NEURAL CORRELATES OF HIGHER COGNITIVE AND EMOTIONAL FUNCTIONS OF THE HUMAN BRAIN

Thesis
presented to the Faculty of Arts
of
the University of Zurich

for the degree of Doctor of Philosophy

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Accepted in recommendation of
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Zurich 2005

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Acknowledgements

Many people contributed to this work and I want to thank all of them. They have been of so much help at various stages of this dissertation project.

My first thanks go to my mentor Prof. Dr. Lutz Jäncke for his supportive scientific supervision. Moreover and most important, he gave me the opportunity to learn different and current essential brain research methods, including functional magnetic resonance imaging (fMRI), electroencephalography (EEG) and transcranial magnetic stimulation (TMS). I am very grateful for having got the chance to acquire practical and theoretical knowledge of these different methods and to work in the fascinating field of human brain research. I also thank Prof. Dr. Lutz Jäncke for our countless and stimulating discussions, for his positive and constructive criticism of my ideas and last but not least for believing in me.

I wish to express my thanks to the members of my dissertation steering committee of the Neuroscience Center Zurich (ZNZ), Prof. Dr. Lutz Jäncke, Prof. Dr. Ulrike Ehlert, Dr. Valentine Marcar and Dr. Markus Heinrichs.

I also want to thank all co-workers of the department of Neuropsychology at the University of Zurich for instrumental and emotional support, in particular Dr. Michaela Esslen and Dr. Kai Lutz for providing tremendous support at the application of the complex neuroimaging methods (EEG and fMRI), Elke Präg and Petra Jäncke for providing emotional support during difficult and sometimes frustrating phases of this dissertation project and Dr. Valentine Marcar for commenting on my English writing.

My thanks also go to my students, Silvia Bach, Lilian Valko and Bigna Lenggenhager for excellent research assistance in conducting and analysing of the experiments, in particular during the Spatial Presence project of this dissertation (Chapter 7). Furthermore, I am grateful to all volunteers for having participated in the studies. Last but not least I thank my parents Gertrud and Walter Baumgartner, who died already 6 years ago, and my two sisters Regula and Andrea for much support over the years.

Summary

The goal of the three empirical brain imaging studies of this dissertation was to elucidate the neural correlate of strong emotional experiences (study A + B) and the neural correlate of Spatial Presence (study C). The three studies will be summarized shortly in the following.

Study A: Most previous neurophysiological studies evoked emotions by presenting visual stimuli. Models of the emotion circuits in the brain have for the most part ignored emotions arising from musical stimuli. This is the first emotion brain study which examined the influence of visual and musical stimuli on brain processing. Highly arousing pictures of the International Affective Picture System and classical musical excerpts were chosen to evoke the three basic emotions of happiness, sadness and fear. The emotional stimuli modalities were presented for 70 seconds either alone or combined (congruent) in a counterbalanced and random order. Electroencephalogram (EEG) Alpha-Power-Density, which is inversely related to activity, in 30 scalp electrodes from 24 right-handed healthy female subjects was recorded. In addition, heart rate (HR), skin conductance responses (SCR), respiration, temperature and psychometrical ratings were collected. Results showed that the experienced quality of the presented emotions was most accurate in the combined conditions, intermediate in the picture conditions and lowest in the sound conditions. Furthermore, both the psychometrical ratings and the physiological involvement measurements (SCR, HR, Respiration) were significantly increased in the combined and sound conditions compared to the picture conditions. Finally, repeated measures ANOVA revealed the largest Alpha-Power-Density for the sound conditions, intermediate for the picture conditions, and lowest for the combined conditions, indicating the strongest activation in the combined conditions in a distributed emotion and arousal network comprising frontal, temporal, parietal and occipital neural structures. Summing up, these findings demonstrate that music can markedly enhance the emotional experience evoked by affective pictures.

Study B: Music is an intriguing stimulus widely used in movies to increase the emotional experience. However, besides the EEG study mentioned above (study A, note that this study only could explore the brain activation of cortical structures with low spatial resolution), no brain imaging study has to date examined this enhancement effect using emotional pictures (the modality mostly used in emotion research) and musical excerpts. Therefore, I designed this functional magnetic resonance imaging (fMRI) study to explore the cortical as well as subcortical structures (with high spatial resolution) of this emotional enhancement effect. In a

classical block design carefully controlling for habituation and order effects, fearful and sad pictures (mostly taken from the International Affective Picture System) were presented either alone or combined with congruent emotional musical excerpts (classical pieces). Subjective ratings clearly indicated that the emotional experience was markedly increased in the combined relative to the picture condition. Furthermore, using a second-level analysis and a regions of interest approach, I observed a clear functional and structural dissociation between the combined and the picture condition. Besides increased activation in brain areas known to be involved in auditory as well as in neutral and emotional visual-auditory integration processes, the combined condition showed increased activation in many structures known to be involved in emotion processing (including for example amygdala, hippocampus, parahippocampus, insula, striatum, medial ventral frontal cortex, cerebellum, fusiform gyrus). In contrast, the picture condition only showed an activation increase in the cognitive part of the prefrontal cortex, mainly in the right dorsolateral prefrontal cortex. Based on these findings, I postulate that emotional pictures evoke a more cognitive mode of emotion perception, whereas congruent presentations of emotional visual and musical stimuli rather automatically evoke strong emotional feelings and experiences.

Study C: Using EEG, psychophysiology and psychometric measures, this is the first study which investigated the neurophysiological underpinnings of Spatial Presence. Spatial Presence is considered a sense of being physically situated within a spatial environment portrayed by a medium (e.g. television, virtual reality). 12 healthy children and 11 healthy adolescents were watching different virtual roller coaster scenarios. During a control session, the roller coaster cab drove through a horizontal roundabout track. The following realistic roller coaster rides consisted of spectacular ups, downs and loops. Low resolution brain electromagnetic tomography (LORETA) and event-related desynchronisation (ERD) were used to analyse the EEG data. As expected, we found that compared to the control condition experiencing a virtual roller coaster ride evoked in both group strong Spatial Presence experiences, increased electrodermal reactions and activations in parietal brain areas known to be involved in spatial navigation. In addition, brain areas were strongly activated which receive homeostatic afferents from somatic and visceral sensations of the body. Most interesting, children compared to adolescents reported higher Spatial Presence experiences and demonstrated a different frontal activation pattern. While adolescents showed increased activation in prefrontal areas known to be involved in the control of executive functions, children demonstrated a decreased activity in these brain regions. Interestingly, recent

neuroanatomical and neurophysiological studies have shown that the frontal brain continues to develop to adult status well into adolescents. Thus, the result of our study implies that the increased Spatial Presence experience in children may result from the not fully developed control functions of the frontal cortex.

The three experimental studies revealed interesting and promising results concerning the neural correlates of strong emotional experiences and Spatial Presence. Nevertheless, additional theoretical and empirical research is necessary in order to investigate these neural correlates in greater detail.

Zusammenfassung

Das Ziel der drei durchgeführten empirischen Gehirnstudien war es, die neuronalen Korrelate von starken emotionalen Empfindungen und die neuronalen Korrelate von Spatial Presence zu ergründen. Diese drei Studien werden im Folgenden kurz zusammengefasst.

Studie A: Die meisten bisherigen gehirnphysiologischen Studien haben versucht, Emotionen mittels visuellen Stimuli zu evozieren. Emotionsstudien, welche versucht haben, Emotionen mittels musikalischer Stimuli zu evozieren, wurden bislang in der Gehirnforschung fast vollständig ignoriert. Dies ist die erste Studie, welche den Einfluss von visuellen and musikalischen Stimuli auf die emotionale Gehirnverarbeitung zum Untersuchungsgegenstand hat. Stark emotionale Bilder vom "International Affective Picture System" und klassische Musikstücke wurden verwendet, um die drei Basisemotionen Freude, Trauer, und Angst zu evozieren. Die emotionalen Stimulus-Modalitäten wurden für 70 Sekunden entweder alleine oder kongruent kombiniert in einer ausgewogenen und pseudo-randomisierten Reihenfolge präsentiert. Um die Gehirnaktivierung zu messen, wurde das Elektroenzephalogramm (EEG) von 30 Elektroden und 24 rechtshändigen, weiblichen Versuchspersonen abgeleitet. Ausgewertet wurde die Power im Alphaband (8-13 Hz), da sie ein guter Indikator für kortikale Aktivierung dargestellt, d.h. Alpha-Power korreliert negative mit kortikaler Aktivierung. Zusätzlich zu den gehirnphysiologischen Massen wurden psychophysiologische Masse erhoben (elektrodermale Aktivität, Herzrate, Respiration, Temperatur) und psychometrische Fragen bezüglich Valenz und körperliche Aktivierung/Erregung mussten beantwortet werden. Die Ergebnisse zeigten, dass die verschiedenen Emotionen am klarsten und genauesten in der kombinierten Bedingung, gefolgt von der Bilder-Bedingung wahrgenommen worden sind. Am wenigsten genau und klar war die Emotionswahrnehmung in der Musik-Bedingung. Sowohl die psychometrischen als auch die psychophysiologischen Aktivierungsmasse (elektrodermale Aktivität, Herzrate, Temperatur) waren signifikant erhöht in der kombinierten und in der Musik-Bedingung im Vergleich mit der Bilder-Bedingung. Zu guter Letzt zeigte sich die höchste Alpha-Power in der Musik-Bedingung, eine mittlere Alpha-Power in der Bilderbedingung und die signifikant niedrigste Alpha-Power in der kombinierten Bedingung. Diese Befunde deuten hypothesenkonform darauf hin, dass die kombinierte Bedingung zur stärksten Aktivierung in einem ausgedehntem neuronalen Emotions- und Aktivierungsnetzwerk führte, welches frontale, temporale, occipitale und parietale Strukturen umfasst. Zusammenfassend zeigen diese Befunde, dass Musik ein starker

emotionaler Stimulus darstellt, welcher die emotionale Verarbeitung von emotionalen Bildern signifikant steigern kann.

Studie B: Musik ist ein wichtiger Stimulus, welcher häufig in Filmen dazu verwendet wird, das emotionale Empfinden zu steigern und zu intensivieren. Ausser der oben erwähnten EEG Studie (Studie A, welche nur die globalen kortikalen Aktivierungsmuster mit niedriger räumlicher Auflösung untersuchen konnte) hat bislang keine gehirnphysiologische Studie diesen emotionalen Verstärkungseffekt mit Bildern und Musikstücken untersucht. Demzufolge wurde diese Studie entworfen, um mittels der funktionellen Magnetresonanztomographie (fMRT) sowohl die kortikalen als auch die subkortikalen Strukturen dieses emotionalen Verstärkungseffektes mit hoher räumlicher Auflösung zu ergründen. In einem klassischen Blockdesign, bei welchem Habituations- und Reihenfolgeeffekte sorgfältig kontrolliert worden sind, wurden angstbesetzte und traurige Bilder (die meisten stammten vom "International Affective Picture System") entweder alleine oder kongruent kombiniert mit emotionalen klassischen Musikstücken präsentiert. Das subjektive Rating der Versuchspersonen zeigte, dass das emotionale Empfinden in der kombinierten Bedingung im Vergleich zur Bilderbedingung signifikant gesteigert war. Gehirnphysiologisch zeigte sich mittels einer "Second-Level" und "Regions of interest" (ROI) Analyse eine klare funktionelle und strukturelle Dissoziation zwischen der kombinierten und Bilderbedingung. Neben erhöhter Gehirnaktivierungen in Strukturen, welche bekanntermassen in auditorische Verarbeitungsprozesse und neutrale als auch emotionale visuell-auditorische Integrationsprozesse involviert sind, zeigte die kombinierte Bedingung eine verstärkte Aktivierung in vielen Strukturen, von denen man weiss, dass sie eine wesentliche Rolle bei der Verarbeitung emotionaler Stimuli spielen, wie zum Beispiel Amygdala, Hippocampus, Parahippocampus, Insula, Striatum, ventromedialer Teil des Frontalkortex, Cerebellum und Gyrus fusiformis. Auf der anderen Seite zeigte die Bilderbedingung nur eine Erhöhung der Aktivierung im kognitiven Teil des präfrontalen Kortex, nämlich vor allem im rechten dorsolateralen Präfrontalkortex. Basierend auf diesen Befunden postuliere ich, dass emotionale Bilder in den meisten Fällen "nur" einen emotionalen und stark kognitiv gefärbten Wahrnehmungsprozess evozieren, während die kombinierte Präsentation von visuellen und musikalischen Stimuli automatisch und ohne grosse kognitive Anstrengung zu starken Gefühlen und Empfindungen führt.

Studie C: Dies ist die erste Studie, welche mittels Elektroenzephalogramm (EEG), Psychophysiologie und psychometrischen Massen versuchte, das neuronale Korrelat von

Spatial Presence zu erforschen. Spatial Presence wird als ein Gefühl angesehen physikalisch in einer virtuellen Realität anwesend zu sein, d.h. ganz in diese virtuelle Realität einzutauchen, wobei das Bewusstsein der realen Welt zumindest für Momente verschwindet. 12 gesunden Kindern und 11 gesunden jungen Erwachsenen wurden verschiedene virtuelle Achterbahnen auf einem Computermonitor präsentiert. Während einer Kontrollbedingung bestand die Achterbahn aus einem horizontalen Rundkurs. Die darauf folgenden realistischen Achterbahnen bestanden aus spektakulären Loopings und Abfahrten. Zwei unterschiedliche Analysemethoden wurden verwendet, um die EEG Daten zu analysieren ("Low resolution brain electromagnetic tomography" und "event-related desynchronisation"). Wie erwartet zeigte sich, dass die realistischen Achterbahnen im Vergleich mit der Kontrollbedingung zu einem erhöhten subjektiven Spatial Presence Erlebnis, erhöhten elektrodermalen Reaktionen und Aktivierungen in parietalen Gehirnstrukturen führten, welche involviert sind in die räumliche Navigationsprozesse. Des Weiteren zeigten insbesondere Strukturen eine starke Aktivierung, welche homöostatische Afferenzen von somatischen und visceralen Empfindungen des Körpers empfangen. Schlussendlich berichteten Kinder ein erhöhtes Spatial Presence Empfinden, welches einherging mit einer unterschiedlichen Aktivierung in frontalen Gehirnstrukturen. Während junge Erwachsene eine erhöhte Aktivierung in präfrontalen Gehirnstrukturen zeigten, welche massgeblich an der Steuerung exekutiver Kontrollfunktion beteiligt sind, zeigten Kinder eine reduzierte Gehirnaktivierung in diesem Hirngebiet. Interessanterweise haben nun neuroanatomische und neurophysiologische Gehirnstudien herausgefunden, dass die Entwicklung im frontalen Hirngebiet erst im jungen Erwachsenenalter abgeschlossen ist. Folglich deuten die Befunde dieser Studie darauf hin, dass das erhöhte Spatial Presence Empfinden bei Kindern durch die noch nicht vollständig ausgereiften Kontrollfunktionen des Frontalkortex zustande kommt.

Die drei experimentellen Studien haben interessante und viel versprechende Befunde in Bezug auf die neuronalen Korrelate von starken emotionalen Empfindungen und Spatial Presence zum Vorschein gebracht. Zusätzliche theoretische und empirische Forschung ist jedoch von Nöten, um diese neuronalen Korrelate noch genauer zu ergründen.

I. INTRODUCTION

The goal of the present dissertation was to elucidate the neural correlates of higher cognitive and emotional functions of the human brain using modern neuroimaging methods, such as functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). The three conducted brain imaging studies are based on two main questions:

1. **What is the neural correlate of strong emotional experiences?**
2. **How can the brain differentiate between reality and virtual reality or between reality and illusion?**

Ad 1: Different induction methods were used in brain research laboratories to evoke positive and negative emotions, including faces (e.g. Esslen, Pascual-Marqui, Hell, Kochi, & Lehmann, 2004; Glascher, Tuscher, Weiller, & Buchel, 2004; Krolak-Salmon, Henaff, Vighetto, Bertrand, & Mauguiere, 2004; Sato, Yoshikawa, Kochiyama, & Matsumura, 2004), pictures (e.g. Lang et al., 1998; Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002; Lee et al., 2004), films (e.g. Lane, Reiman, Ahern, Schwartz, & Davidson, 1997; Aalto et al., 2002; Moran, Wig, Adams, Jr., Janata, & Kelley, 2004; Reiman et al., 1997), sounds (Sander, Brechmann, & Scheich, 2003; Sander & Scheich, 2001), music (e.g. Blood & Zatorre, 2001; Blood, Zatorre, Bermudez, & Evans, 1999), words (Smith & Bulman-Fleming, 2005; Schapkin, Gusev, & Kuhl, 2000) and recall of autobiographical life events (Damasio et al., 2000; Mayberg et al., 1999).

However, the modality mostly used in emotion brain research is vision and in the majority of these studies either the International Affective Picture System by Lang, Bradley and Cuthbert (1995) or the Picture of Facial Affect by Ekman and Friesen (1976) have been used as emotional stimulus material. In contrast, emotions evoked by other modalities and in particular musical stimuli in the auditory modality are completely understudied. Emotional appreciation of music is a new research avenue in neuropsychology and neurophysiology (Peretz, 2001). Nevertheless, the results of the few existing studies are remarkable. For example, Blood and Zatorre (2001) have shown that musical stimuli alone elicited strong emotional responses that activated brain regions known to be involved in reward/motivation, emotion and arousal, including ventral striatum, thalamus, midbrain, orbitofrontal cortex and insula.

However, it is obvious that real-life emotional experiences mostly rely on the presence of combined stimuli coming from different modalities. For example, music is often used to enhance the emotional impact of movies. Although this enhancing effect of combined presentation of emotional music and visual stimuli is intuitive and well-known, modern neuroimaging research has completely ignored the neurophysiological underpinnings of this enhancement effect, i.e. no study to date has ever explored this emotional enhancement effect using musical and visual emotional stimuli.

Therefore, two studies were designed and conducted to explore this emotional enhancement effect using pictures of the International Affective Picture System (Lang, Bradley, & Cuthbert, 1995) and classical musical excerpts. Both stimuli modalities were presented either alone or congruent combined in a counterbalanced and random order. In one study, EEG was used to measure the implicated cortical structures of this enhancement effect along with psychometrical and psychophysiological (heart rate, skin conductance responses, temperature, respiration) measures and in the other study, fMRI was used to measure cortical as well as subcortical structures (not possible using EEG) along with psychometrical measurements. I hypothesized that the combined presentation of congruent emotional stimuli compared to the single presentations leads to (1) increased psychometrical intensity ratings, (2) increased somatic and visceral body reactions (e.g. heart rate, skin conductance responses) along with (3) enhanced activation in brain structures known to be involved in emotion processing. The findings of these studies therefore help to discriminate between a network of brain structures involved in strong emotional experiences and a network of brain structures involved in a more cognitive, less arousing emotional perception process.

Ad2: In the context of the second main question of this dissertation project I deal with the phenomenon of "Spatial Presence". Spatial Presence can arise in virtual realities and is considered as “sense of being there” which “occur when part or all of a person’s perception fails to accurately acknowledge the role of the technology that makes it appear that s/he is in a physical location and environment different from her/his actual location and environment in the physical world” (Schubert, Friedmann, & Regenbrecht, 2001). Or in other words, it is the illusion or experience that the virtual reality environment is real and not virtual. Thus, the perceptual system of our brain is generating a percept making us believe that we see something real although it is unreal. Although this percept is common to all people it has received little attention in neuroscientific research. To date, only psychometrical (e.g. Freeman, Avons, Pearson, & Ijsselsteijn, 1999; Ijsselsteijn, de Ridder, Freeman, Avons, &

Bouwhuis, 2001; Robillard, Bouchard, Fournier, & Renaud, 2003) and a few psychophysiological studies (e.g. Meehan, 2001; Meehan, Insko, Whitton, & Brooks, 2002; Wiederhold, Jang, Kim, & Wiederhold, 2002b) have examined this phenomenon. No brain activation study has ever explored the neural underpinnings of Spatial Presence. The ignorance towards this concept is especially surprising because it tackles a yet unsolved question, namely how the brain distinguishes between reality and virtual reality or between reality and illusion.

Therefore, EEG along with psychophysiological (heart rate and skin conductance responses) and psychometrical measures was used to explore the neural underpinnings of Spatial Presence in an arousing and emotional virtual reality environment. Children (age 7-10) and adolescents (age 14-17) were watching different virtual roller coaster scenarios. During a control session, the virtual roller coaster drove through a horizontal roundabout track with only a few spatial cues. During the experimental session, the roller coaster rides consisted of spectacular ups, downs and loops and thus consisted of many spatial cues. I hypothesized that the experimental compared to the control condition should evoke (1) stronger Spatial Presence experiences, (2) increased somatic and visceral reactions of the body and (3) a different brain activation pattern, including at least increased activation in the parietal lobe known to be involved in spatial processing (e.g. Jordan, Schadow, Wuestenberg, Heinze, & Jancke, 2004; Jordan, Wustenberg, Heinze, Peters, & Jancke, 2002; Jordan, Heinze, Lutz, Kanowski, & Jancke, 2001). Moreover, I also expected that children compared to adolescents report an increased Spatial Presence experience along with a different brain activation pattern, mainly in the prefrontal lobe due to the following reasons. Recent neuroanatomical and neurophysiological studies have shown that the frontal brain continues to develop to adult status well into adolescents (Giedd et al., 1999; Giedd, 2004). Moreover, the frontal lobe is known to be highly involved in the executive control system of the brain, including for example monitoring and error detection (Smith & Jonides, 1999). Thus, I hypothesized that based on the incomplete functioning of this control centre of the brain younger children are more prone to experience strong Spatial Presence.

The findings of this study not only can help to discriminate between brain structures involved in high Spatial Presence experience and low Spatial Presence experience, but rather can help to elucidate brain areas involved in the discrimination of reality, virtual reality and illusion.

At first sight, the discussed two main projects of this dissertation do not seem to have much in common. However, at second sight, one can discover some interesting communalities. First,

both projects try to evoke strong emotional experiences along with increased somatic and visceral reactions of the body. Therefore, one can postulate that in spite of the different paradigms a similar network of brain structures should be activated in both projects which constitutes a neural correlate of strong emotional experiences. Second, in both projects low emotional and low Spatial Presence experiences are evoked as well. Again, it is interesting to observe if similar brain areas are active in both projects which diminish the emotional experience as well as the Spatial Presence experience.

Briefly, the present dissertation provides a broad summary of research about emotion and Spatial Presence with special accentuation on brain imaging studies. Moreover, two major research projects (3 studies) on the neural correlate of strong emotional experiences and high Spatial Presence are presented and the empirical results are critically discussed with respect to possible explanations for the observed findings from recent literature.

The first part of the dissertation (Theoretical Part) is devoted to a literature review about emotion processing (Chapter 1), Spatial Presence (Chapter 2) and the two brain imaging methods used in this dissertation, namely functional magnetic resonance imaging and electroencephalography (Chapter 3). More precisely, Chapter 1 reviews the literature about models of emotion processing (Chapter 1.1), emotional appreciation of music focusing brain imaging studies (Chapter 1.2) and crossmodal integration of emotional faces and voices (Chapter 1.3). Note that no brain imaging study has ever explored the crossmodal integration of emotional pictures and musical excerpts. Finally, I discuss in Chapter 1 the difference between emotion perception and emotion experience, i.e. the difference between a more cognitive, less arousing emotional perception process and a more arousing emotional perception process leading to strong emotional feelings (Chapter 1.4). Chapter 2 begins with a definition of the concept of Spatial Presence (Chapter 2.1) and gives a literature review about media and user factors fostering Spatial Presence (Chapter 2.2), models of Spatial Presence focusing a psychological and a neuropsychological model (Chapter 2.3), and the few existing psychophysiological studies (Chapter 2.4). Note that no study has ever examined the neural correlate of Spatial Presence. Therefore, only peripheral physiological studies can be discussed. Finally, based on general human lesion and human neuroimaging studies I discuss the potentially involved cortical and subcortical structures in the process of Spatial Presence (Spatial Presence and the brain, Chapter 2.5). Chapter 3 is devoted to a literature review about theoretical principles, preprocessing and statistical analysis of the two brain imaging methods

used in this dissertation, namely the functional magnetic resonance imaging (Chapter 3.1) and the electroencephalography (Chapter 3.2). The second part of the book (Empirical Part) is devoted to the three empirical studies of this dissertation (Chapter 4-7) and the general discussion of all three studies (Chapter 8). In detail, Chapter 4 briefly discusses the general aims of the three studies. Chapter 5 and 6 discusses two studies (an EEG and fMRI study) which tried to elucidate the neural, psychophysiological and psychometrical underpinnings of strong emotional experiences evoked by emotional visual and musical excerpts. Thereafter in Chapter 7, the findings of an EEG study exploring for the first time the neural correlates of Spatial Presence is presented. In addition to EEG, psychometrical as well as psychophysiological measures were obtained in a non-interactive, arousing virtual reality world depicting different roller coaster rides. Finally in Chapter 8, the pivotal findings of the experimental studies are summarized (Chapter 8.1) and discussed focusing similarities regarding processes of strong emotional experiences (Chapter 8.2) as well as processes of controlling and modulating these strong feeling states (Chapter 8.3). At the end, a short conclusion and outlook for future studies is given (Chapter 8.4).

II. THEORETICAL PART

1 Emotion

1.1 Models of emotion processing

Different theories of emotion processing have been proposed. Until now, two major classes of psychological theories of emotion dominated research in cognitive neuroscience: (1) basic emotions theories and (2) dimensional theories. Recently, instead of adopting either the *discrete emotions* or the *dimensional views*, some researchers have adopted an alternative and promising approach. This approach takes into consideration the complexity of emotion by parsing its subcomponents at the process-level and determining interactions between the proposed processes. These multicomponent models of emotion processing based on theoretical elements as well as empirical data (animal, human lesion and human neuroimaging studies) have recently received much attention. Therefore, the two former theories will be only discussed briefly and the main discussion is focussed on the multicomponent models of emotion processing and implicated cortical and subcortical structures.

1.1.1 Basic emotions theories

Most of the past cognitive neuroscience research on emotion focused on the attempt to find specific brain regions implementing distinct basic emotions such as happiness, sadness, disgust, anger, fear, and surprise (see Ekman, 1999) which are reflected in human facial expressions across cultures. However, the findings are discrepant and there is to date only limited empirical support for this theory. For example, it has been proposed that the insula is particularly involved in processing "disgust" (Phillips et al., 1997; Calder, Lawrence, & Young, 2001) and that the amygdala is specifically implicated in the processing of fear-related stimuli (Mineka & Ohman, 2002; Ohman & Mineka, 2001). However, challenging this "basic emotion" approach, the insula was also found to be activated during the experience of sadness (George, Ketter, Parekh, Herscovitch, & Post, 1996), fear conditioning (Buchel, Dolan, Armony, & Friston, 1999), processing fearful as compared to neutral faces (Anderson, Christoff, Panitz, De, & Gabrieli, 2003a), and processing of positive emotions (e.g. humor apprecation, Moran et al., 2004). Similarly, amygdala activation was reported to a wide variety of positive and negative emotional stimuli, including fear faces (Morris et al., 1996; Phillips et al., 1997), aversive pictures (Taylor et al., 1998; Simpson et al., 2000), sad (Blair, Morris, Frith, Perrett, & Dolan, 1999) and happy faces (Breiter et al., 1996; Pessoa, McKenna,

Gutierrez, & Ungerleider, 2002), positive pictures (Hamann, Ely, Grafton, & Kilts, 1999; Garavan, Pendergrass, Ross, Stein, & Risinger, 2001), film excerpts (Aalto et al., 2002; Reiman et al., 1997), as well as positive (laughing) and negative (crying) sound stimuli (Sander et al., 2003; Sander et al., 2001). Therefore, it appears that the insula as well as the amygdala are not specifically involved in disgust-related and fear-related mechanisms, respectively.

However, there is some evidence from a recent meta-analysis of neuroimaging studies (Phan, Wager, Taylor, & Liberzon, 2002) that the amygdala is more often engaged in the processing of fear-related stimuli than in the processing of any other emotion and that the emotion of sadness is associated with activity in the subcallosal cingulate (Liotti et al., 2000; Mayberg et al., 1999).

In addition, convergent findings from functional neuroimaging studies have clearly demonstrated the existence of brain regions specialized for reward processing initially suggested by studies showing that rats responded operantly to stimulation of specific sites to the exclusion of other activities (Olds & Milner, 1954). These neuroimaging studies have highlighted the role of the ventral striatum in craving (Breiter et al., 1997), in the time-locked processing of reward prediction (Pagnoni, Zink, Montague, & Berns, 2002), in anticipation of reward (Knutson, Fong, Adams, Varner, & Hommer, 2001), and in romantic love (Bartels & Zeki, 2000) as well as happiness-induced recall (Damasio et al., 2000), sexual arousal (Rauch et al., 1999) and pleasant pictures (Lane et al., 1997; Davidson & Irwin, 1999).

1.1.2 Dimensional theories

Another tradition has considered that emotions are represented in a common multidimensional space. For example, Wundt (1905) proposed that the nature of an emotion is defined by its position within three orthogonal dimensions: pleasantness-unpleasantness, rest-activation, and relaxation-attention. Anderson et al. (2003b) argued that the cognitive neuroscience of emotion should consider that emotional response and stimulus evaluation are primarily characterized by two dimensions: valence (negative-positive) and intensity (low-high). Thus, Anderson et al. (2003b) found that amygdala was associated with intensity but not valence of odors, whereas distinct regions of orbitofrontal cortex were associated with valence independent of intensity. Similary, Small (2003) dissociated regions responding to taste intensity and taste valence: structures such as the middle insula and the amygdala coded intensity irrespective of valence, whereas other structures such as the orbitofrontal cortex showed valence-specific responses.

1.1.3 Multicomponent appraisal theories

Scherer (2000) combined theoretical elements for which one can find an increasing consensus in the literature and proposed the following multicomponent process model of emotion. According to this model, an emotion involves a sequence of state changes in each of the five following components: (1) appraisal, (2) motivation or action tendencies, (3) motor expression, (4) autonomic processes, and (5) subjective feeling.

Phillips et al. (2003) proposed a similar model of emotion processing. According to this model emotion processing can be understood in terms of the following processes occurring after the initial presentation of an emotive stimulus: (1) the appraisal and identification of the emotional significance of the stimulus; (2) the production of a specific affective state in response to the stimulus, including autonomic, neuroendocrine, and somatomotor (facial, gesture, vocal, behavioural) responses, as well as conscious emotional feeling; (3) the regulation of the affective state and emotional behaviour, which may involve an inhibition or modulation of processes 1 and 2, so that the affective state and emotional behaviour produced are contextually appropriate (see Figure 1.1).

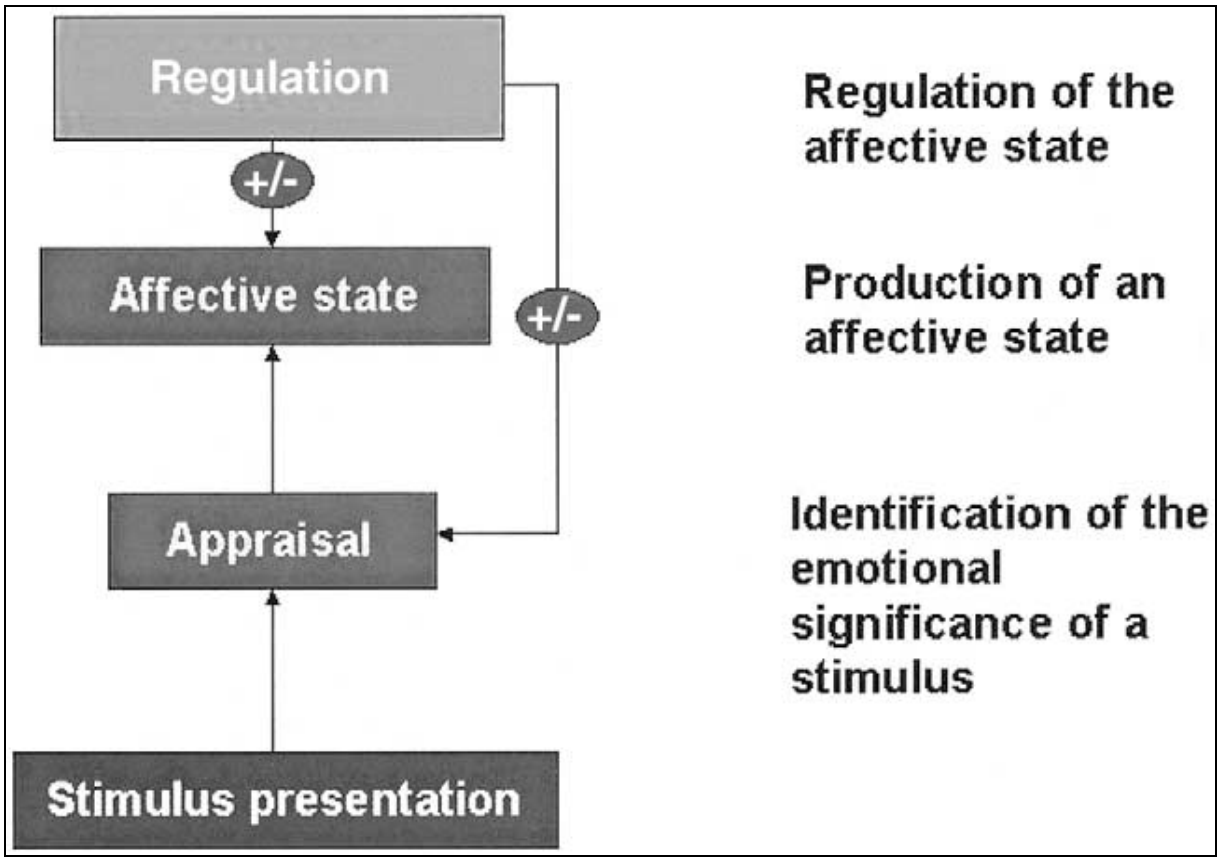

Figure 1.1: Model of emotion processing proposed by Phillips et al. (2003)

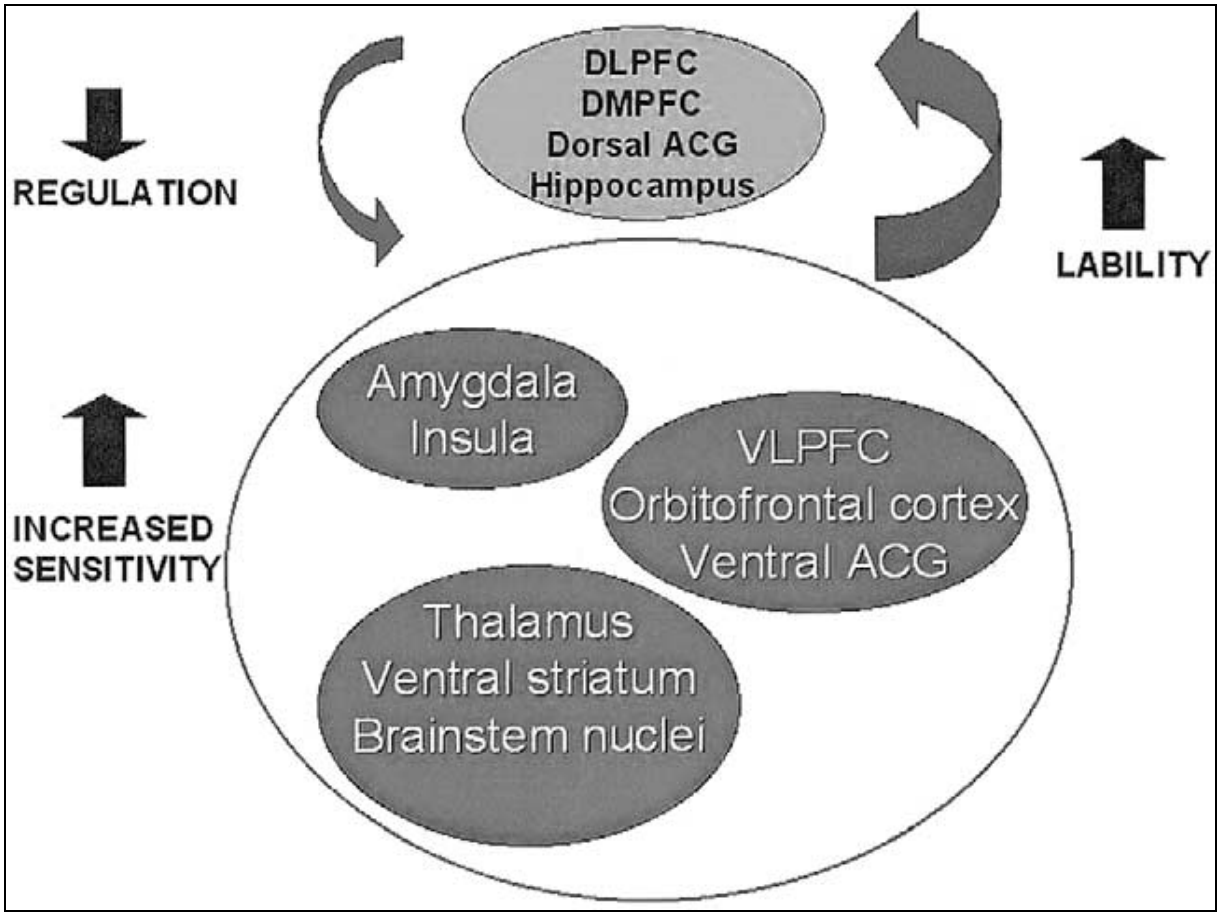

Figure 1.2: Schematic diagram depicting neural structures important for the three processes underlying emotion processing according to the model of Phillips et al. (2003). A predominantly ventral system is important for the identification of the emotional significance of a stimulus, the production of an affective state, and autonomic response regulation (depicted in dark gray), whereas a predominantly dorsal system (depicted in pale gray) is important for the effortful regulation of the resulting affective states. A reciprocal functional relationship may exist between these two neural systems (curved arrows). VLPFC, ventrolateral prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; DMPFC, dorsomedial prefrontal cortex; ACG, anterior cingulate gyrus.

Moreover and most interesting, the same research group (Phillips, Drevets, Rauch, & Lane, 2003) proposed based on recent animal, human lesion, and functional imaging studies that the described three processes are dependent upon the functioning of two neural systems: a ventral system, including the amygdala, insula, ventral striatum, thalamus, brainstem nuclei and ventral regions of the anterior cingulate gyrus and prefrontal cortex, predominantly important for processes 1 and 2 and automatic regulation of emotional responses; and a dorsal system, including hippocampus and dorsal regions of the anterior cingulate gyrus and prefrontal

cortex (dorsolateral prefrontal cortex and dorsomedial prefrontal cortex), predominantly important for process 3 (see Figure 1.2).

Taken together, the postulated model suggests that the extent to which a stimulus is identified as emotive and is associated with the production of an affective state and/or emotional behaviour may be dependent upon levels of activity within a ventral system, important for the rapid appraisal of emotional material, production of affective states, and autonomic response regulation, and a dorsal system, important for effortful regulation of resulting affective states.

1.2 Emotional appreciation of music

Models of the emotion circuits in the brain have for the most part ignored emotions arising from musical stimuli. However, there is extant literature examining the psychology and peripheral psychophysiology of emotion in music.

1.2.1 Psychological studies

Psychological studies show that listeners are quite consistent in associating basic or primary emotions such as happiness, sadness, fear, and anger to musical compositions (e.g. Cupchick, Rickert, & Mendelson, 1982; Hevner, 1936; Nordenstreng, 1968; Wedin, 1972). Ordinary adult listeners need less than a quarter of a second of music to reliably distinguish the tone of the whole musical excerpts as happy or sad (Peretz, Gagnon, & Bouchard, 1998). It is also remarkable how skilled the young children are in emotional perception. From the age of three years, they show the ability to recognise happiness in elaborate art music of their culture, and by the age of six they show adult-like abilities to identify sadness, fear, and anger in music (Cunningham & Sterling, 1988; Terwogt & van Grinsven, 1988; Terwogt & van Grinsven, 1991). The happy and sad emotional tones tend to be among the easiest to communicate in music (e.g. Gabrielsson & Juslin, 1996; Krumhansl, 1997). Moreover, the major structural determinants of the happy-sad distinction are well identified: tempo and mode. Fast tempi tend to evoke a happy tone, whereas slow tempi tend to evoke a sad tone. Similarly, the major mode is associated with happiness and the minor mode is associated with sadness (Peretz et al., 1998).

1.2.2 Peripheral psychophysiological studies

The extant literature examining the psychophysiology of emotion in music has primarily focused on peripheral physiological measures. For example, there are documented relations between music and autonomic measures. Thayer and Levenson (1983) found that music added to stressful films was related to changes in skin conductance levels. Still more recent studies

have noted changes in peripheral physiological measures during the presentation of different affective music excerpts. Krumhansl (1997) noted that sad excerpts produced the largest changes in heart rate, blood pressure, skin conductance, and temperature; fear excerpts produced the largest changes in blood transit time and amplitude; happy excerpts produced the largest changes in respiration measures. Khalfa et al. (2002) indicated that skin conductance responses (SCR) were found to be greater with the more stimulating musical emotions, fear and happiness, as compared to the two more relaxing emotions, sadness and peacefulness.

1.2.3 Brain activation studies

1.2.3.1 Cognitive processing

Studies of the central processing of musical stimuli have focused primarily on cognitive aspects such as rhythm, pitch, contour, and expectancy. What is clear from these studies is that many areas of the brain including frontal, temporal, and parietal regions are involved in music processing (Samson & Zatorre, 1992; Trainor, Desjardins, & Rockel, 1999). In a recent review Zatorre, Belin and Penhune (2002) argued that there is a relative specialisation of the auditory cortices in the two hemispheres, such that temporal resolution is better in left auditory cortical areas and spectral resolution is better in right auditory cortical areas. Speech is highly dependent on rapidly changing broadband sounds, whereas tonal patterns tend to be slower, although small and precise changes in frequency are important. With respect to speech processing, a vast body of data indicates that certain aspects of speech decoding depend critically on left auditory cortical regions (e.g. Binder et al., 2000; Hickok & Poeppel, 2000; Jancke, Wustenberg, Scheich, & Heinze, 2002). On the other hand, relative specialisation within right auditory regions for tonal processing (music) is supported by functional imaging data from a wide variety of perceptual tasks (e.g. Zatorre, Evans, & Meyer, 1994; Penhune, Zattore, & Evans, 1998). Therefore, Zatorre et al. (2002) propose that cortical asymmetries might have developed as a general solution to the need to optimize processing of the acoustic environment in both temporal and frequency domains.

1.2.3.2 Emotional processing

With respect to emotion there are only a few studies which analyzed the influence of emotional musical excerpts on the central processing in the brain. Nevertheless, the results of these few studies are remarkable.

Blood, Zatorre, Bermudez, and Evans (1999) used positron emission tomography to examine cerebral blood flow (CBF) changes related to affective responses to music. Ten volunteers were scanned while listening to six versions of a novel musical passage varying

systematically in degree of dissonance. Regional CBF changes in paralimbic and neocortical areas were associated with both increasing dissonance and increasing consonance. However, distinct structures were activated by dissonance versus consonance. Activity in right parahippocampal gyrus and precuneus regions correlated with increasing dissonance, whereas activity in orbitofrontal, subcallosal cingulate and frontal polar cortex correlated with decreasing dissonance (equivalent to increasing consonance).

In an other study, Blood and Zatorre (2001) examined the neural mechanisms underlying intensely pleasant emotional responses to music. Cerebral blood flow changes were measured in response to subject-selected music that elicited the highly pleasurable experience of "shivers-down-the-spine" or "chills". All music selections were of the classical genre, and included pieces such as Rachmaninoff's *Piano Concerto No. 3 in D Minor, Opus 30, Intermezzo Adagio,* and Barber's *Adagio for Strings*. All subjects were musicians and subjective reports of chills were accompanied by increases in heart rate, electromyogram, and respiration. Furthermore, as intensity of these chills increased, cerebral blood flow increases were observed in the ventral striatum, insula, thalamus, midbrain, orbitofrontal cortex and anterior cingulate, whereas decreased blood flow were observed in the amygdala, the hippocampus and ventromedial prefrontal cortex and visual cortex. These brain regions are thought to be involved in reward/motivation, emotion, and arousal and moreover, the pattern of brain activation is similar to that observed in brain imaging studies of euphoria and/ or pleasant emotion (e.g. Breiter et al., 1997; Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001). For example, activity in the ventral striatum (nucleus accumbens), thalamus, insula, and anterior cingulate cortex has been reported to increase, and in the amygdala and ventromedial prefrontal cortex to decrease, in response to cocaine administration in cocaine-dependent subjects (Breiter et al., 1997). This finding links music with biologically relevant, survival-related stimuli via their common recruitment of brain circuitry involved in pleasure and reward. In a recent PET study (Brown, Martinez, & Parsons, 2004), the results of the study by Blood et al. (2001) were replicated with non-musicians who were passively listening to unfamiliar instrumental music. Strongly pleasant feelings were associated with increased activation in the subcallosal cingulate gyrus, prefrontal anterior cingulate, retrosplenial cortex, hippocampus, anterior insula, and nucleus accumbens.

Schmidt and Trainor (2001) examined whether the pattern of regional EEG activity distinguished emotions induced by musical excerpts of fear, joy, happiness and sadness in a group of undergraduates. They found that the pattern of asymmetrical frontal EEG activity distinguished valence of the musical excerpts. Subjects exhibited greater relative left frontal

EEG activity to joy and happy musical excerpts and greater relative right frontal EEG activity to fear and sad musical excerpts. They also found that, although the pattern of frontal EEG asymmetry did not distinguish the intensity of the emotions, the pattern of overall frontal EEG activity did, with the amount of frontal activity decreasing from fear to joy to happy to sad excerpts. Subsequently, the same group of researchers (Tsang, Trainor, Santesso, Tasker, & Schmidt, 2001), using the same EEG technique, were able to replicate and relate the EEG findings to musical structure. They observed that changes in both tempo and mode in the happier direction resulted in greater relative left frontal activation, whereas changes in both tempo and mode in the sadder direction resulted in greater relative right frontal activation.

In a recent study Altenmüller, Schürmann, Lim, and Parlitz (2002) also confirmed this lateralisation effect which has been proposed by Davidson and his colleagues more than 25 years ago (Davidson, Schwartz, Saron, Bennett, & Goleman, 1979; for an recent review see Davidson, 2003; Davidson et al., 1999). They investigated the neurobiological mechanisms accompanying emotional valence judgements during listening to complex auditory stimuli. Students listened to 160 short sequences taken from the repertoires of jazz, rock-pop, classical music and environmental sounds. Emotional valences of the perceived stimuli were rated on a 5-step scale after each sequence. Brain activation patterns during listening revealed widespread bilateral fronto-temporal activation, but a highly significant lateralisation effect: positive emotional attributions were accompanied by an increase in left temporal activation, negative by a more bilateral pattern with preponderance of the right fronto-temporal cortex. No differences related to the four stimulus categories could be detected, suggesting that the actual auditory brain activation patterns were more determined by their affective emotional valence than by differences in acoustical “fine” structure.

Taken together, these few emotional brain studies and in particular the three described neuroimaging studies have clearly demonstrated that musical stimuli can evoke strong emotional experiences.

1.3 Crossmodal integration of emotional faces and voices

No behavioural and neuroimaging study in the literature has ever explored the crossmodal integration effect of congruent emotional musical and visual stimuli. However, a few behavioural and neuroimaging studies exists which explored this crossmodal integration effect regarding emotional face and voice stimuli. The subsequent sections will discuss these studies.

1.3.1 Behavioural studies

Psychological data indicate that bimodal or multimodal inputs are important in emotional perception. For example, when subjects view emotional faces in combination with emotional voices, information from both modalities is combined in making affective judgements. This means, that a fearful face is more likely to be perceived as fearful if accompanied by a fearful voice (Massaro & Egan, 1996). Furthermore, evidence for crossmodal emotional perceptual effects is provided by experiments where pairing an emotional face with a congruent emotional voice leads to a facilitation in facial emotional recognition (de Gelder & Vroomen, 2000). Crossmodal effects in perception of emotion are also evident in infants who dwell longer on a face when accompanied by an emotionally congruent, as opposed to an incongruent voice (Walker & Grolnick, 1983). Finally, when the expression in the voice and the face are congruent, subjects are faster at judging the expression than when they only receive one input. This gain in response latencies for bimodal congruent stimuli provides evidence for the notion that perceivers integrate the two sources of information and that this integration is automatic and mandatory (Massaro et al., 1996; de Gelder et al., 2000)

1.3.2 Brain activation studies

The first study which directly addressed the integration question (Dolan, Morris, & de, 2001) used fMRI and revealed stronger activation in the amygdala and the fusiform gyrus in the congruent emotional condition (congruent fearful faces and voices) compared to the incongruent condition (fearful face and happy voice). A recent fMRI study (Pourtois, de, Bol, & Crommelinck, 2005) extended the research carried out by Dolan and collaborators (2001) by introducing single modality conditions in order to obtain insight into the difference between each single modality separately and the combination. They presented fearful and happy Pictures of Facial Affect (Ekman & Friesen, 1976) and fearful and happy voices (speaking a word) either alone (single modality condition) or congruent combined (fearful faces with fearful voices and happy faces with happy voices). The results indicated that the perception of audio-visual emotions (fear and happiness) activates the left medial temporal lobe relative to unimodal conditions and the left fusiform gyrus. The medial temporal gyrus is known to be involved in multisensory integration and brain damage to the temporal polar cortex impairs emotional recognition of both facial and vocal stimuli (Adolphs, Damasio, & Tranel, 2002; Adolphs, 2002). The activation of the fusiform gyrus is consistent with results from the fMRI study of Dolan et al. (2001). However, activation in the amygdala was obtained for fearful faces and fearful audio-visual pairs but not for fearful voices only,

indicating no enhanced processing in the amygdala in the bimodal compared to both unimodal conditions.

Taken together, the few behavioural und neuroimaging studies indicate a clear emotional enhancement effect in the combined compared to the single modality conditions. This enhancement is demonstrated by increased activations in brain areas known to be involved in multisensory integration (medial temporal gyrus), modality-specific sensory processing (fusiform gyrus) and emotion processing (amygdala) along with facilitation in emotion facial recognition and gain in response latencies.

1.4 The difference between emotion perception and emotion experience

In this section, criteria are discussed which help to objectively discriminate between processes of cognitively evaluating emotions (emotion perception) on the one hand and processes of feeling and experiencing emotions (emotion experience) on the other hand.

1.4.1 Somatic and visceral body reaction

For a long time there had been a passionate debate in psychology between the centralist and the peripheralist views, the latter arguing that the source of emotions lies in the peripheral nervous system. Representatives of the peripherialistic view (starting with James, 1884; and Lange, 1885) assumed that there are emotional experiences, i.e. feelings, because changes in the peripheral or visceral nervous system are perceived, the so-called James-Lange theory. Simplified: because we notice the chances in our physiological parameters (e.g. higher pulse rate, skin conductance responses, or respiration) we develop the corresponding emotion (e.g. fear, sadness). Although soon criticized by Cannon (1927) and Bard (1929), there were periodically modified and refined revivals of this concept (e.g. Schachter, 1962; Zillman, 1978), which maintained the idea that emotions are cognitive interpretations of somatic body sensations. Nowadays, there is hardly any discussion that emotions are generated directly in the brain. Somatic and visceral body reactions are simple to slow to be the origin of emotions (Cannon, 1927).

Nevertheless, recent research have strongly supported the idea that somatic and visceral body reactions are not the origin of emotions, but an important aspect for the subjective process of feeling emotions (Damasio et al., 2000; Craig, 2002). On the basis of neurological analyses of patients with forebrain lesions, Antonio Damasio (Damasio, 1994) has advanced the “somatic marker” hypothesis of consciousness. He proposes that the subjective process of feeling emotions requires the participation of brain areas that are involved in the mapping and/or regulation of our continuously changing internal states – that is, in homeostasis. These

feelings help to guide behavioural decisions that affect survival and quality of life by producing a perceptual landscape that represents the emotional significance of a particular stimulus that is being experienced.

Taken together, these findings indicate that emotional experiences or feelings are accompanied by somatic and visceral reactions of the body along with activations in brain areas involved in the mapping and/or regulation of these body reactions. The following section will discuss the implicated cortical and subcortical structures.

1.4.2 Structures implicated in strong emotional feelings

Damasio et al. (2000) reported a PET study that brings strong support for his "somatic marker" theory (see Chapter 1.4.1). The subjects had to generate emotions by recalling autobiographical life events. They were instructed to re-experience as intensively as possible episodes in which they felt sadness, happiness, anger and fear. A neutral episode without any feelings but recalled in the same way was used as control condition. Somatic body reactions (skin conductance responses, heart rate) and psychometrical intensity ratings were all significantly enhanced in all emotional conditions compared to the neutral condition. In addition, all emotions engaged structures related to the representation and/or regulation of organism state, including the insula, the secondary somatosensory cortex, the cingulate cortex and nuclei in brainstem and hypothalamus. All these regions share a major feature in that they are all direct or indirect recipients of signals from the somatic and visceral state of the body (Davidson et al., 1999; Craig, 2002).

These findings are consistent with other brain imaging studies that have associated activation of structures mapping and regulating the state of the body, in particular the insula (see Figure 1.3), with strong subjective emotional feelings, such as anticipatory anxiety and pain (Ploghaus et al., 1999), humour appreciation (Moran et al., 2004) disgust (Phillips et al., 1997), sexual arousal (Stoleru et al., 1999) and subjective responses to music (Blood et al., 2001). Nonetheless, it is equally important to recognize that other structures as the anterior cingulate cortex and the orbitofrontal gyrus as well as the amygdala and the striatum were co-activated in most of these studies.

Interestingly, all brain structures which showed increased activation during strong emotional experiences are part of the ventral system for emotion processing proposed by Phillips et al. (2003, see chapter 1.3) which is important for the identification of the emotional significance of a stimulus and the production of affective states, including autonomic, neuroendocrine, and somatomotor responses and conscious feelings. Notably, no structure of the cognitive dorsal system for emotion processing was associated with strong emotional feelings. Therefore, one

can conclude that strong emotional experiences compared to more cognitive emotional perception processes are associated with (1) increased psychometrical intensity ratings, (2) increased somatic and visceral reactions of the body (e.g. skin conductance responses, heart rate), and (3) increased activation in brain structures known to be involved in the ventral system for emotion processing and in particular in the mapping and/or regulation of the somatic and visceral reactions of the body, such as the insula and the secondary somatosensory cortex.

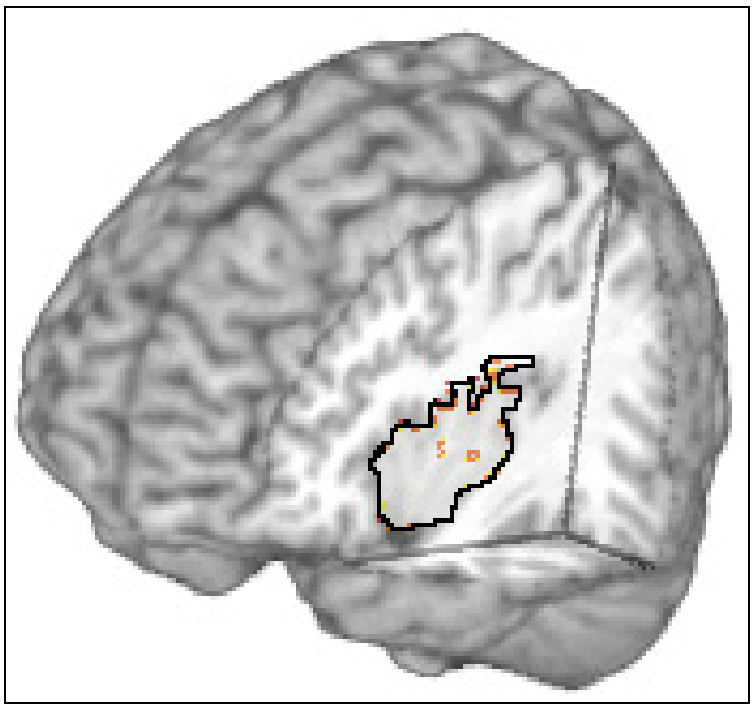

Figure 1.3: 3D view of the human brain. Depicted in white color is the left insular cortex which forms the medial limit of the lateral sulcus. This structure is thought to play a major role during processes of strong emotional feelings by mapping and regulating the somatic and visceral state of the body.

> *"When the curtain swept up to reveal the now-legendary wide-screen roller coaster ride, I realized that the film's creators were no longer content to have me look at the roller coaster, but were trying to put me physically on the ride. The audience no longer surrounded the work of art; the work of art surrounded the audience – just as reality surrounds us. The spectator was invited to plunge into another world. We no longer needed the device of identifying with a character on the other side of the 'window'. We could step through it and be a part of the action!"*
>
> *Morton Heilig commenting on his experience with Cinerama in New York, 1952.*

2 Spatial Presence

2.1 Definition

As Heilig's quote illustrates, there has long been a tendency to reproduce reality with increasing level of fidelity, especially in the arts and in cinema, and nowadays in computer-based virtual realities. The psychological effect that Heilig described is these days more commonly known as Presence or Spatial Presence. Spatial Presence is an important variable in numerous fields of communication applications, such as telemedicine (e.g. Westwood, Hoffman, Robb, & Stredney, 1999), entertainment (Klimmt & Vorderer, 2003), education (Psotka, 1995), and psychotherapy (Harris, Kemmerling, & North, 2002). Spatial Presence is considered as "sense of being there" which "occur when part or all of a person's perception fails to accurately acknowledge the role of the technology that makes it appear that s/he is in a physical location and environment different from her/his actual location and environment in the physical world"(Schubert et al., 2001). In contrast to this definition, Wirth et al. (2005, submitted) conceived the term "technology" in a broader meaning, i.e. not only including electronic media like virtual reality technology, but all kinds of media. Consequently, Spatial Presence is defined as a status when part or all of a person's perception fails to acknowledge the role of the media that makes it appear that s/he feels attendant in mediated environment, i.e. an environment that is created by perception of spatial cues of the media content, not by cues of the real physical world. Based on this definition, television, radio, virtual reality technology and even books should be able to produce Spatial Presence in different ways. VR-technology, for example, ensures high interactivity by giving the user possibilities to change her/his field of view, as well as to interact in and with the media environment (Schubert et al., 2001; Schubert, Friedmann, & Regenbrecht, 1999). The numbers of sensory channels addressed by the virtual environment and triggered by specific VR-interfaces are relevant for sensory engagement, motor engagement, and sensorimotor engagement (Biocca, 2001). These different kinds of bodily actions enhance the user's feeling of embodiment in the media

environment, respectively, the feeling of being part of this environment. But if bodily actions would be the only possibility to experience mediated environments, no other medium - besides VR-technology - would be relevant for coming along with Spatial Presence. The „book problem“(Schubert, 2002) describes the phenomenon that the feeling of „being there“ is also connected to books, or, more precisely, to the reading of texts. Although readers are not obviously able to explore and to act in the environment described in a book, they can at least *imagine* acting in the book's world. However, one can assume that the more senses are activated by the media environment, the higher the chance to feel as being in a real environment.

Accordingly, the sense of Presence can vary in degree (Ijsselsteijn, de Ridder, Hamberg, Bouwhuis, & Freeman, 1998): Presence does not occur when a technology user's perceptions fully and accurately acknowledge the role of technology in an experience (e.g., a television viewer might accurately perceive that s/he is watching a human-made technology and that the images on the small box in her/his living room are merely representations of objects, events, and people that may or may not exist elsewhere). Presence is greater, but not maximized, when a technology user's perceptions only partially acknowledge the actual role of technology in the experience (e.g., the user of an advanced virtual reality system may simultaneously be consciously aware of - i.e., think about - the nature of the technology that is generating her/his experience, accurately acknowledging the technological channel through which the experience has been generated, but nevertheless also perceive that s/he is inside the technology-generated environment). Presence is maximized when a technology user's perceptions fail to accurately acknowledge any role of the technology in the experience (e.g., the user of a sophisticated flight simulator may, at least for short periods, be completely unaware of the technological channel through which the experience has been generated and perceive that s/he is actually flying an aircraft). However, although it appears that Presence is a continuous rather than dichotomous variable, it has not been empirically determined whether 1) Presence can exist in varying degrees at each instant (as it seems) or 2) our sense that Presence is continuous is the result of the cumulative effect of instants, which may be as short as milliseconds, in which Presence either does or does not exist (Ijsselsteijn, 2002).

Moreover, the exact nature and location of the processing that results in Presence is not known. It is likely that our initial and immediate responses to external stimuli (i.e., sensations) are identical when the external stimuli are created by or filtered through technology and when the external stimuli are not created by or filtered through technology (i.e., the role of technology is not acknowledged in the former situation). It may be that in some cases

processing continues "automatically" and the possible role of technology in generating the experience is not evaluated, while in other cases a "higher order" or "active" or "conscious" evaluation is made regarding the possible role of technology (a role which may or may not be accurately recognized). It may be that parallel streams of processing occur during perception, so that when we have a sense of Presence we simultaneously acknowledge the role of technology in one stream and fail to do so in another, thus we can be "aware" that we are using a technology (e.g., a virtual reality system) but simultaneously perceive objects, entities, and events we encounter (e.g., sharp objects, avatars, etc.) as if no technology was involved (Ijsselsteijn, 2002). It is also possible that people encourage or discourage their own sense of Presence by directing their attention away from aspects of their experience that serve to remind them of the role of technology in it (Bystrom, Barfield, & Hendrix, 1999).

2.2 Media and user factors fostering Spatial Presence

Based mostly on theoretical analysis and a few empirical findings various user and media factors have been suggested in the literature which are thought to underlie the Spatial Presence experience. These factors are summarized in the following and include:

- *The extent and fidelity of sensory information* – this is the amount of useful and salient sensory information presented in a consistent manner to the appropriate senses of the user. This includes Steuer's (1995) notion of 'vividness', i.e. the ability of a technology to produce a sensorially rich mediated environment. Note that this factor can apply to both interactive and non-interactive media. Examples from this category are monocular and binocular cues to spatial layout, resolution, number of addressed sensory channels, field of view, or spatialized audio. For example, various empirical studies showed that a bigger field-of-view (e.g. Hendrix & Barfield, 1996), monocular (motion parallax) as well as binocular (stereoscopic presentation) spatial cues (e.g. Ijsselsteijn et al., 1998; Freeman et al., 1999), and spatialized audio (stereo and six-channel reproduction, Vastfjall, 2003) lead to more intense experiences of Presence. Furthermore, Dinh, Walker and Hodges (1999) demonstrated empirically that the experience of Presence is increased with the number of sensory channels involved (e.g. one hears an explosion, sees the flash, and smells the smoke simultaneously).
- *The match between sensors and the display* – this refers to the sensory-motor contingencies, i.e. the mapping between the user's actions and the perceptible spatio-temporal effects of those actions. For example, using head tracking, a turn of the user's head should results in a corresponding real-time update of the visual and

auditory display. Empirical evidence for the importance of the match between sensors and the display or between afferent and efferent feedback comes from an investigation conducted by Slater, Usoh and Steed (1995) who found out, that moving through a virtual environment by actually walking and thus moving the own legs and feet leads to higher degrees of Presence than navigating by using an "artificial" hand-held pointing device.

- *Content factors* – this is a broad category including objects, actors, and events represented by the medium, and the user's ability to interact with and modify the content of a mediated environment (Sheridan, 1992).The object is assumed to be more realistic and meaningful if it is scaled in a proper way, if it is colored and textured in accordance with the user's expectations and perceptual hypotheses (Slater, 2002) and if it shows an adequate autonomous behaviour. For example, it has been shown that Presence reported by chess players increases when chess pieces are arranged in meaningful positions as compared to random arrangements (Hoffman, Prothero, Wells, & Groen, 1998). Note that in virtual environments the parts of the user's virtual body can be regarded as objects that should be presented properly, too (Heeter, 1992). Finally, virtually all Presence related publications that cover theoretical issues have addressed interactivity as an important factor that contributes to the experience (e.g. Ijsselsteijn, 2002; Zahorik & Jenison, 1998).
- *User characteristics* are also likely to play a significant role in users' sensation of Presence, but to date have received little attention. Such characteristics include a user's perceptual, cognitive and motor abilities (e.g. susceptibility to motion sickness, concentration), prior experience with and expectations towards mediated experiences, mood state, and personality, including in particular a concept labelled "suspension of disbelief" (Bystrom et al., 1999). Suspension of disbelief allows the user to "cheat" while the mediated reality is perceptually tested by applying the following strategies: (1) Users actively suppress contradictory information completely, (2) the assessment of contradictory information is disabled, and (3) contradictory information is interpreted as actually supporting the mediated reality. Relevant individual characteristics, including the suspension of disbelief, are likely to vary with the age, and possibly with the sex, of the user. Furthermore, Huang and Alessi (1998) point out that various mental health conditions, such as depression, anxiety, or psychotic disorders, are also likely to affect an individual's sense of Presence, since they affect individuals' experiences around them.

In the Spatial Presence study of this dissertation (see Chapter 7) both media (spatial cues) as well as user factors (the age of the user) have been experimentally manipulated.

2.3 Models of Spatial Presence

2.3.1 Psychological Model

Based on the discussed media and user factors, Wirth et al. (2005) proposed a psychological "Two-level model of the formation of Spatial Presence" (see Figure 2.1). Both levels can be influenced by media as well as user factors.

On the first level, the media users build a mental representation of the space that is portrayed by the media product, called Spatial Situation Model (SSM). Automatic and or/ voluntary attention allocation is a precondition to the construction of the SSM, and media factors such as attention-catching content features and spatial cues (monocular and binocular) as well as user variables such as domain-specific interest and spatial visual imagery will affect the process of its development. If for example, the content of the media product matches the domain-specific interest of a given receiver (e.g. a virtual roller coaster is presented and the user likes riding roller coasters in real life), his/her attention to attend to the media product will increase. Stimuli of the non-mediated environment are 'faded out', whereas stimuli of the mediated environment remain focused. Accordingly, during reading, Presence cannot arise without motivational processes (such as domain-specific interest), because reading is an active procedure that may hardly be sustained without motivation. On the other hand, a virtual realty environment may automatically attract users' attention, which diminishes the role of motivational processes towards the experience of Presence.

Once the user has constructed an SSM, perceptual hypotheses are activated (second level of the model). In case of persuasive media offerings and or/high involvement of the media users, the receivers test the so-called "medium-as-primary-ego-reference-frame hypothesis" which states that the spatial environment represented in the media-based SSM is the primary-ego-reference-frame (PERF). A primary-ego-reference-frame is defined as a mental model of the world that is organized from a first-person perspective (Carlson, 1999; Sholl, 1999). If the hypothesis that the medium is the primary-ego-reference-frame is perceptually confirmed, Spatial Presence emerges, because by accepting (consciously or unconsciously) the mediated space as primary-ego-reference-frame, media users position themselves and realized action possibilities within that space. Both media factors (e.g. persistence, realism) and user actions (involvement, suspension of disbelief) can affect the transition from the SSM to Spatial Presence. For example high-absorptions individuals display tendencies to become intensely

involved with objects (such as media products), and enter the condition of being 'fascinated' without much effort (Wild, Kuiken, & Schopflocher, 1995). Absorption is therefore considered to be correlated positively with attention allocation, the identification of spatial structures, involvement, and in particular suspension of disbelief, as all of these processes are connected to states of fascination and experiential involvement. Accordingly, as both media-induced and user-induced routes to Spatial Presence occur during media exposure, they may compensate for the shortcomings of obstacles on the 'route': Insufficient spatial cues of the media product may be counteracted by users' involvement and suspension of disbelief, and in turn, a lack of user motivation to experience Spatial Presence may by overruled by persuasive and convincing media characteristics.

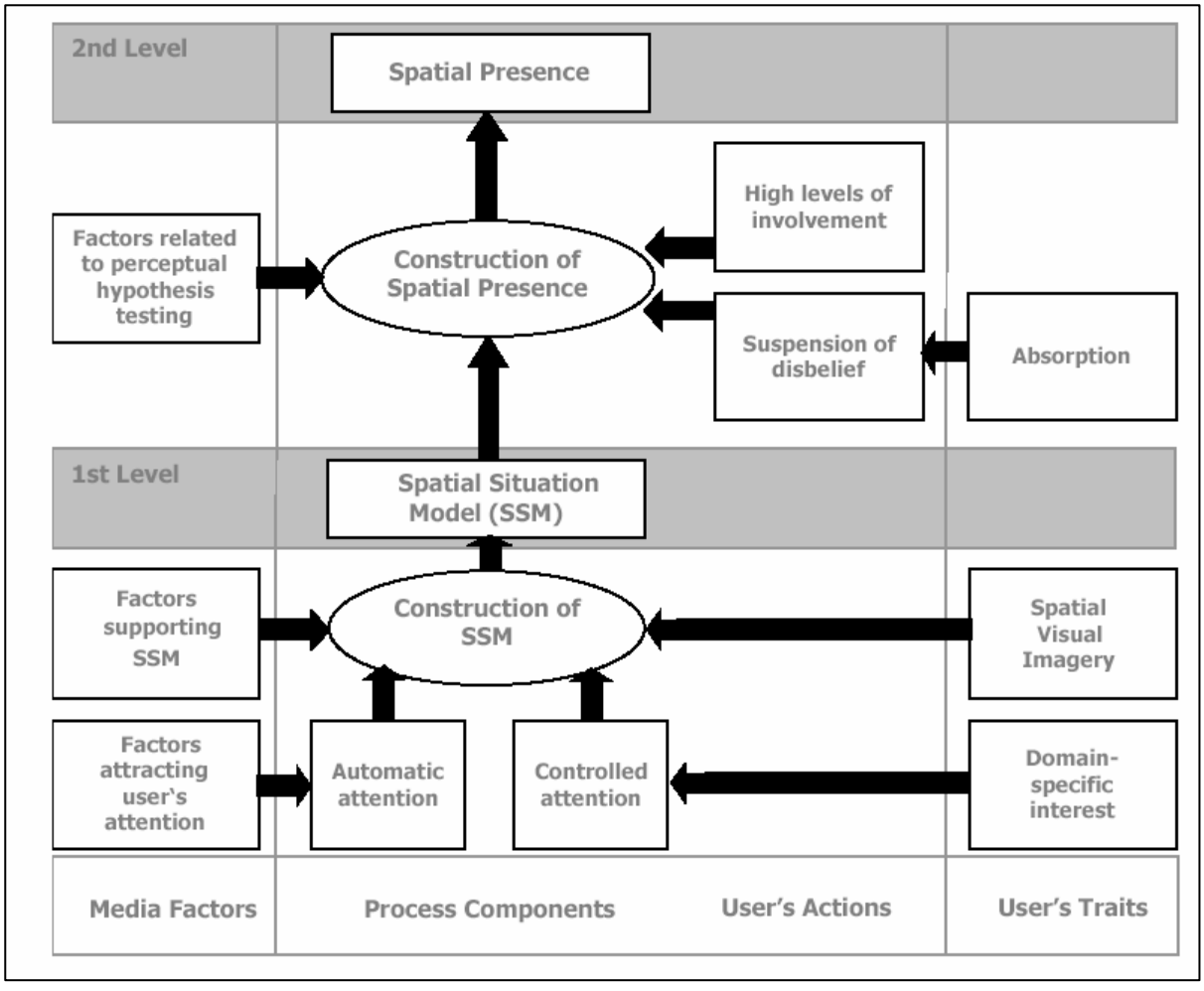

Figure 2.1: Two-level Model of the formation of Spatial Presence (please see text for explanation)

2.3.2 Neuropsychological Model

Based on human lesion, human neuroimaging and transcranial magnetic stimulation (TMS) studies, Jancke (2005, submitted article) formulated the first tentative neuropsychological model of the formation of Spatial Presence. In the following subsection, this model will be summarized. In this model Jancke proposed two neural mechanisms important in the formulation and experience of Spatial Presence. One is called the "reality check" mechanism and the other is called the "intensity check" mechanism. Both mechanisms are important for the brain in the real world to discriminate between imagined and real perceptions or to discriminate between reality and illusion.

The "reality check" is related to the concept named "Reafferenzprinzip" originally proposed by von Holst and Mittelstaed (1950) and later reformulated by Hein and Held (1962). The basic principles of this model is that lower-order modules (e.g. primary auditory cortex) transfer their information to a specific mechanism meant to predict the outcome of the higher-order modules (e.g. association areas in the auditory cortex, i.e. secondary or tertiary auditory cortex). This mechanism can be a kind of "temporary matching storage" in which "representations" between afferent information coming from the lower-order modules are related to expected outcomes. For example, if a specific set of afferent information is currently generated in the primary auditory cortex, the predictive mechanism predicts the expected pattern of higher-order percept. The predicted percept is compared with the actual percept generated by the higher-order modules. This prediction and comparison process is active automatically (with no need of high processing demands) on many levels of this bottom-up process (from the primary sensory cortex to the higher order modules).

However, more interesting, this process can also operate from higher-order neural modules down to lower-order modules (top-down). For example, in situations when we imagine seeing a picture, higher-order modules of the visual processing stream are generating an image which activates the subordinate correlation storage predicting the "afferent" information which normally evokes this image or percept. The predicted afferent information is compared with the actual information. If there is a discrepancy between both, the brains knows that the image is generated by higher-order modules and does not depend on physically present information. Interestingly, there are several neurological diseases in the auditory and visual system where this discrimination mechanism between reality and imagined reality (or illusion) is strongly disturbed. Such diseases are the Charles Bonnet syndrome and the acquired deafness (Heilman & Valenstein, 2003). Patients suffering from the Charles Bonnet syndrome have damages in their peripheral visual pathway causing complete or partial blindness, whereas

patients suffering from acquired deafness have lost their ability to hear because of multiple heterogeneous reasons. Paradoxically, many of these patients start experiencing extremely vivid hallucinations in the visual and auditory modality, respectively. For example, Charles Bonnet patients have hallucinations of extended landscapes scenes or disembodied and distorted faces with prominent eyes and teeth (Santhouse, Howard, & ffytche, 2000), whereas patients with acquired deafness have musical hallucinations, including classical music, pop music or other kinds of music (Griffiths, 2000). Although these hallucinations are different, they all have one feature in common, that is the vivid nature and the perceived reality of these hallucinations. Griffiths (2000) examined the brain activation of six patients with acquired deafness and observed a positive correlation between brain activation and severity of hallucinations in the secondary auditory cortex as well as within the association areas of the frontal lobe, basalganglia and the cerebellum. However, no increased activation was found in the primary auditory cortex.

The proposed and discussed "reality check" mechanism can very nicely explain why Charles Bonnet patients and deaf patients suffering from musical hallucinations generate vivid hallucinations which can hardly be distinguished form real experiences. In these patients there is either no afferent information or degraded information available from lower-order modules. Therefore, these patients cannot use incoming information to compare afferent information with the predicted "afferent" information. The discrepancy between both afferent signals will be large in all situations making it useless for further processing purposes. Thus, the brain has to reorganize the way it processes and interprets the images generated by higher-order-modules. Jancke (2005) proposes that in these situations the discrimination between reality and illusion is relying exclusively or predominantly on the second discrimination mechanism, namely the "intensity check" and thus, the vividness of the generated image.

That the intensity of activation within a processing module determines the vividness of a perceived image or hallucination has nicely been shown by several experiments using functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS) or by using intracortical stimulation techniques. In a recent fMRI study by Bartels and Zeki (2004) it was demonstrated that there is a high positive linear correlation between the intensity of the subjective experience of certain stimulus feature (e.g. color, faces, human body) with the activity in the higher-order areas specialized for it. Moreover, it has been consistently shown that these specialist areas may be active even when there is no conscious percept of the attribute they process (Dehaene et al., 2001; Moutoussis & Zeki, 2002; Zeki & ffytche, 1998). These findings indicate that the amount of activity in an area directly reflects

the intensity of the percept of the attribute it is specialized for, and that, however, a certain minimal amount of activity is required to achieve a percept.

Further confirmation for the "intensity check" mechanism comes from TMS studies. TMS applied over the extrastriate areas evoke visual illusions (called phosphenes) in most subjects if the TMS impulses are evoked outside the vicinity of the primary visual cortex with reasonable high intensity (Fernandez et al., 2002; Amassian et al., 1998). More interesting, increasing the TMS intensity up to a specific level increases also the vividness of the perceived visual hallucination. A further fascinating example for the importance of the activation level of a specific module has been given in a very recent paper (Blanke, Landis, Spinelli, & Seeck, 2004). In this study the authors report extraordinary findings from an epileptic patient whom intracortical electrodes were implanted in the inferior parietal lobe region (in the angular gyrus of the right hemisphere) for diagnostic reasons. Applying electrical impulses to this area evoked a kind of "out-of-body" experiences in these patients. Moreover, the patient reported more bizarre and vivid "out-of-body" experiences with increasing intensity of the electrical stimulation.

Jancke (2005) emphasises that increasing the electrical stimulation (either with TMS or intracortical stimulation) mostly increases the neurophysiological activation level in the stimulated region and therefore, the level of neurophysiological intensity can be considered as an important variable to distinguish between images or perceptions driven by higher-order or lower-order modules. In case of high neural intensity levels in higher-order modules accompanied by vivid illusions the brain might decide that these images are "real" and may originate from physically present stimuli. An everyday example for this "intensity check" mechanism comes from 3D movies shown in IMAX cinemas or roller coaster movies. Some of these movies are of such a quality that the audience moving in the chair in front of the movie screen as if they were sitting in a real seat within a roller coaster. For example, when the roller coaster in the movie is making a fast right turn, the viewer is also bending his body to the right although he/she is actually sitting on a fixed underground.

Both "reality check" and "intensity check" need a threshold to decide if the generated percept is driven by physically present stimuli or not. These thresholds depend on subjective experiences, motivations, personality and may vary over time (e.g. may be different in children and adolescents). Both mechanisms are operative in healthy persons. However, the "intensity check" mechanism is the dominant mechanism which can override the "reality check" mechanism. In terms of Spatial Presence that means that the generation of Spatial Presence is high when (1) higher-order modules show strong activation and (2) the "reality

check" mechanism and involved structures show diminished activation or is completely disabled. Accordingly, this model predicts that multimodal stimuli are more suitable to evoke strong Spatial Presence experiences than unimodal stimuli. In addition, multimodal stimuli comprising stimuli moving in a biologically relevant manner are most suitable to evoke Spatial Presence. As discussed in Chapter 2.2, both predictions of the model were confirmed in the Presence literature using psychometrical and behavioural methods (see for example Dinh, Walker, & Hodges, 1999; Ijsselsteijn et al., 2001). However, no study has ever directly explored the neural underpinnings of Spatial Presence and therefore, the predictions of the model concerning the neural activation of brain structures await confirmation.

2.4 Psychophysiological studies

A number of physiological indicators, such as heart rate and skin conductance response (SCR), have been suggested as objective measures of Presence, but at present there is little empirical research available that is specifically aimed at relating physiological measures to Presence. According to Meehan (2001) physiological Presence means that a user is "responding physiologically to the mediated environment in a manner consistent with human response to similar real situations". For example, when the content of the mediated environment is not arousing, there is no reason to expect that psychophysiological measures would increase, even if there would be high sense of Presence. In contrast, if a virtual reality is filled with highly arousing violent, threatening or sexual content, a high sense of Presence should be accompanied by a notable increase in psychophysiological arousal measures. And therefore, psychophysiological measures are a useful indicator of increased Presence. Note that it has been suggested that mediated stimuli that evoke a high sense of Presence are often also arousing (Lombard & Ditton, 1997).

Heart rate and skin conductance responses (SCR) have been recently used in a number of studies examining Spatial Presence in virtual reality worlds (participants were wearing head-mounted displays). For example, Meehan showed that SCR and heart rate were positively associated with self-reported Presence during exposure to a pit room with an unguarded hole in the floor leading to a room 20 ft. below (Meehan et al., 2002). Furthermore, it was also found that SCR and heart rate were higher during exposure to the frightening (i.e. arousing) virtual height situation compared to a non-frightening virtual room. In contrast, Wiederhold et al. (1998) found that change in heart rate correlated negatively and change in SCR positively with self-reported Presence when participants were presented with a virtual environment depicting an airplane flight. The contradictory finding concerning heart rate can easily be

explained. Whereas in the study by Meehan et al. the virtual environment (pit room) was stressful enough to elicit a sympathetically-mediated defense response and therefore a heart rate acceleration, the virtual environment used in the study by Wiederhold et al. (1998) elicited increased attention as indexed by parasympathetically-mediated HR deceleration, well known as orienting response (e.g. Schandry, 1996).

The virtual environment depicting an airplane flight was also used to investigate the physiological reaction of nonphobic and phobic participants (Wiederhold et al., 2002b). As a result, SCR showed significant differences between nonphobics and phobics, respectively. Interestingly, the physiological responses of the 33 phobic participants, who were able to fly without medicine after virtual reality treatment, showed a gradual trend toward the nonphobics' physiological responses as therapy sessions progressed. Moreover, Wiederhold (2002a) demonstrated that this virtual reality graded exposure therapy was more efficacious than imaginal exposure therapy in the treatment of fear of flying (DSM-IV diagnosis of specific phobia of fear of flying). Only one participant (10%) who received imaginal exposure therapy and 90% of participants who received virtual reality exposure therapy reported an ability to fly without medication or alcohol at three-month followup.

Taken together, the few existing psychophysiological studies indicate that physiological measures are useful as an objective measure of Spatial Presence in arousing virtual reality worlds.

2.5 Spatial Presence and the brain

Based on the two presented models of Spatial Presence (see Chapter 2.3.1 and 2.3.2.), I will discuss in the following the potentially involved cortical and subcortical structures in the formation and experience of Spatial Presence in an arousing, but non-interactive virtual reality world. The virtual reality world used in the Spatial Presence study of this dissertation is non-interactive (subjects are watching from the ego-perspective roller coaster rides), as is the same experience in the real world. I have chosen this non-interactive virtual reality because I wanted to explore the neural correlates of Spatial Presence not confounded by cognitive or motor processes which are of course strongly activated in an interactive virtual reality world where subjects can freely move around (by using electronic devices or actually using their own legs) and have to interact with the surrounding environment. Because no study has ever directly explored the neural underpinnings of Spatial Presence neither in an interactive nor in a non-interactive virtual reality, only tentative hypothesis concerning the involved cortical and subcortical structures can be formulated.

2.5.1 Parietal Cortex and spatial processing

Recent human neuroimaging studies have delineated the brain areas involved in various spatial processing tasks. These studies have shown that the intrapartietal sulcus (IPS, see Figure 2.2) region and adjacent areas in the parietal lobe (including the superior parietal lobe) play a pivotal role during spatial processing of mental rotation (e.g. Jordan et al., 2002; Jordan et al., 2001) or navigation tasks in virtual mazes (e.g. Jordan et al., 2004; Gron, Wunderlich, Spitzer, Tomczak, & Riepe, 2000).

More interesting, two different strategies have been proposed in the navigation literature to solve such navigation tasks: the egocentric and the allocentric strategy. Subjects using the egocentric strategy use meaningful landmarks (local focus) to navigate through 3D environments. They orient themselves as if they were within the 3D environment and they learn the location of specific targets and how often they turn right or left. In contrast, subjects using an allocentric strategy make use of mental spatial maps. A pivotal aspect of the latter strategy is that the subjects orient themselves according to general landmarks (global focus) like direction (north or south) or the position of the sun. These two strategies have neural correlates in different parts of the brain. Whereas activation in the aforementioned parietal cortex and in particular in the right parietal cortex reflects the egocentric space representation frame, activation in the medial temporal lobe system (and mainly in the hippocampus) provides an allocentric representation of locations, or a cognitive map of the environment (Jordan et al., 2004; Maguire et al., 1998; Mellet et al., 2000).

The first person view of the egocentric strategy is generated by translation of the retinal coordinates to head-centered, or even body-centered, coordinates (Burgess, Jeffery, & O'Keefe, 1999). Obviously, this first person, egocentric view is tightly connected with the experience of Spatial Presence. Therefore, one can postulate that Spatial Presence can not arise without activation in the parietal cortex and mainly in the areas surrounding the intraparietal sulcus. I suggest that in the terminology of the discussed psychological "Two-Level Model of Spatial Presence" (see Chapter 2.3.1), the activation in the parietal cortex is called the formation of the Spatial Situation Model (SSM), which is, according to the model, a necessary but not sufficient prerequisite for the experience of Spatial Presence. This proposal seems to be in line with brain activation data showing that not every activation in the intraparietal sulcus leads automatically to the experience of Spatial Presence. For example, as stated above, mental rotation figures can also activate this brain area and this cognitive task seems indeed not extremely suitable to evoke Spatial Presence. However, based on the "intensity check" proposed in the model of Jancke (2005, see Chapter 2.3.2), it would also be

conceivable that a certain activation threshold must be achieved in this brain area to evoke the experience of Spatial Presence. Most probably, a strong activation in this important brain area along with a specific pattern of activation and deactivation in other brain areas constitutes the neural correlate of Spatial Presence (please see next sections for the discussion of other structures).

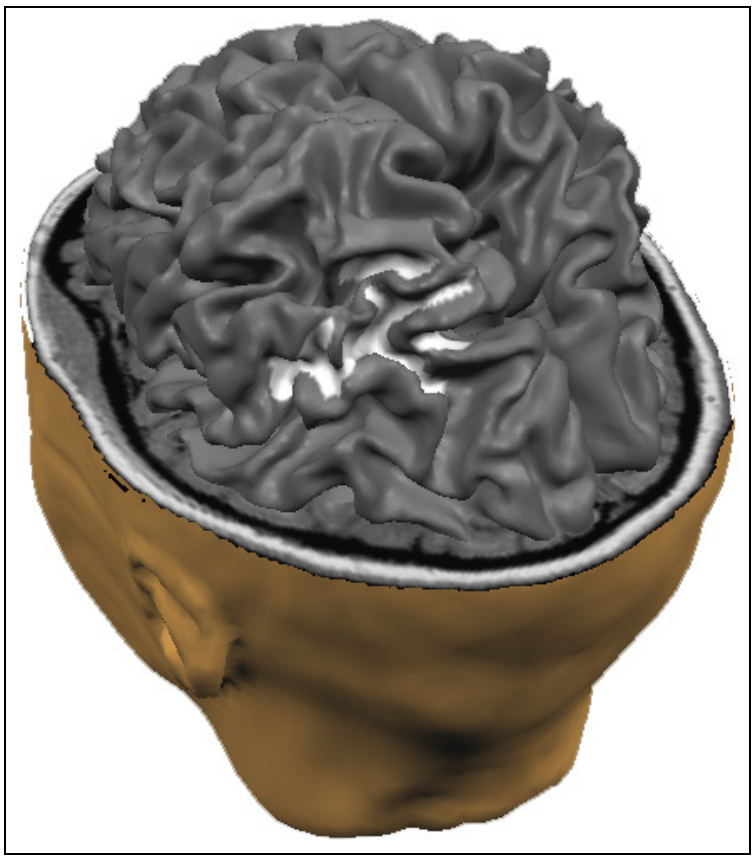

Figure 2.2: Depicted in white color is the left intraparietal sulcus which is surrounded by the superior parietal gyrus and the inferior parietal gyrus.

2.5.2 Prefrontal cortex and executive function

Both discussed models propose control mechanisms to discriminate between reality and virtual reality called “reality check” and “intensity check” in the model of Jancke (2005, see Chapter 2.3.2) and called “perceptual hypothesis testing” in the model of Wirth (2005, see Chapter 2.3.1). One potential structural candidate playing a pivotal role in this control processes is the prefrontal cortex (see Figure 2.3) known to be highly involved in the executive control function of the brain, including mechanisms relating to (a) attention and inhibition, (b) task management, (c) planning, (d) monitoring and (e) coding (Smith et al., 1999). Obviously, these processes and in particular processes of attention and inhibition as well as monitoring are involved in the formation and experience of Spatial Presence.

Moreover, Philipps (2003) proposed a functional distinction between more dorsal regions and more ventral regions of the prefrontal cortex. Whereas the dorsal part (including the dorsal

anterior cingulate cortex) is mainly involved in cognitive processing, the ventral part of the prefrontal cortex (including the ventral anterior cingulate cortex) is mainly involved in emotional processing. For example, the dorsolateral prefrontal cortex has been implicated in many cognitive functions, including monitoring and manipulation with working memory (Owen, 1997; Petrides, 1994), response selection (Rowe, Toni, Josephs, Frackowiak, & Passingham, 2000) and the implementation of strategies to facilitate memory (Bor, Duncan, Wiseman, & Owen, 2003). The dorsal anterior cingulate has been implicated in error and performance monitoring (Carter et al., 1998), in conflict processing (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999) and in difficult task performance (Paus, Koski, Caramanos, & Westbury, 1998). In contrast, the ventral part of the frontal cortex and in particular the orbitofrontal cortex has been implicated in processes that involve the motivational or emotional value of incoming information, including the representation of primary (unlearned) reinforcers such as taste, smell and touch (Tataranni et al., 1999; Gottfried, O'Doherty, & Dolan, 2002; Rolls, 2000) and the representation of learnt relationships between arbitrary neutral stimuli and rewards or punishments (Tremblay & Schultz, 1999; Rolls, Critchley, Browning, & Hernadi, 1998). Finally, the ventral part of the anterior cingulate cortex is known to be involved in the processing of emotional information during arousal and the production of affective states (Esslen et al., 2004; Mayberg et al., 1999; Shin et al., 2000).

Based on these findings, I suggest that the experience of Spatial Presence in an arousing virtual reality world is enhanced by activation in the ventral part of the prefrontal cortex or at least not reduced, but disturbed by activation in the dorsal more cognitive part of the prefrontal cortex. Subjects who cognitively evaluate the virtual environment and search for errors or conflicts in the virtual reality reduce their Presence experience. In contrast, subjects showing diminished activation in the cognitive dorsal system of the prefrontal cortex should report an increased Spatial Presence experience. For example, to cognitively avoid feeling anxious phobic subjects could block Presence during a virtual reality exposure therapy by attending to cues that underline the merely virtual nature of the phobogenic stimuli. Empirical evidence that this avoidance is associated with activation in the dorsal part of the prefrontal cortex comes from neuroimaging studies. A recent study demonstrated that the intensity and unpleasantness during pain stimulation correlated positively with activation in the ventral part of the prefrontal cortex (orbitofrontal gyrus), while a negative correlation was found with activation in the dorsolateral prefrontal gyrus (Lorenz, Minoshima, & Casey, 2003). Moreover, in a recent meta-analysis of 55 neuroimaging studies of emotion processing Phan et al.(2002) found that emotional studies with a cognitive task (e.g. emotion-labeling, gender

discrimination) were about 20% more numerous in demonstrating activation in the dorsal anterior cingulate and dorsal prefrontal gyrus, whereas emotional studies without cognitive task were approximately 15% more numerous in demonstrating activation in subcortical structures (including the amygdala and hippocampus).

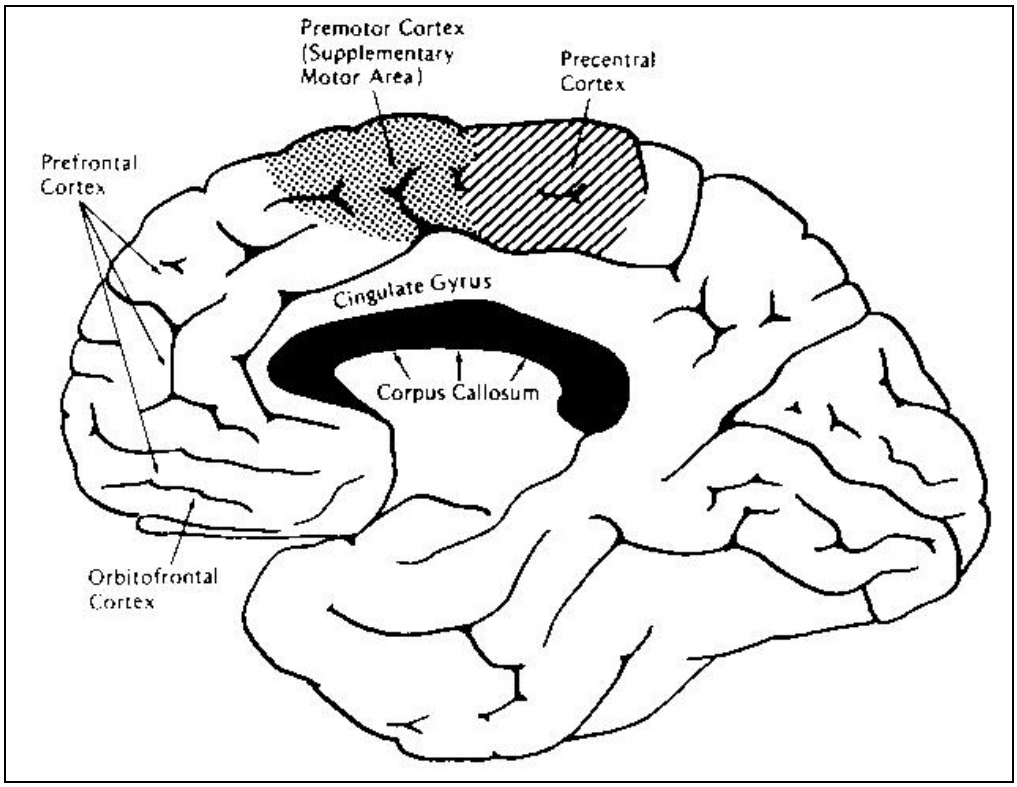

Figure 2.3: Depicted is a medial view of the human brain. Anterior to both the premotor and precentral cortex lies the prefrontal cortex, which makes up most of the frontal cortex and encompasses the pole of the lobe (Heilman et al., 2003).

Another interesting finding concerning the relationship of Spatial Presence and activation in the prefrontal lobe has recently been postulated. Based on neuroimaging studies, Corbetta and Shulman (2002) proposed a right lateralized frontoparietal attention network. This network, including mainly the middle and inferior frontal cortex as well as the temporo-parietal junction, works as an alerting system, directing attention to behaviourally relevant sensory stimuli that are outside the focus of attention. In the context of Spatial Presence this alerting system is very interesting for the following reasons. To enhance the Spatial Presence experience, the focus of attention should obviously be directed to the virtual reality world and the sensory stimuli outside the focus of attention, in this case the real world, should not or less be processed (for example a telephone call). However, it is in the nature of things that this alerting system works automatically and unconsciously because it is important for an organism to monitor the environment (in this case the real world) continuously for potentially

significant information, even this information is not relevant for the ongoing action (in this case the virtual reality). For instance, in order to survive animals must clearly be capable of responding to the unexpected appearance of say, a predator, with a fast "task switch" from the ongoing activity (e.g. eating) to a very different behaviour (e.g. flight). Therefore, this alerting system as well as other cognitive processes of the prefrontal cortex (e.g. error monitoring) can not be completely suppressed and therefore reduce the Spatial Presence experience.

However, as postulated in both models, media factors (e.g. persistence, realism) as well as user factors (e.g. personality, age, motivation) can affect this control mechanism, i.e. either enhance the activation or decrease the activation of these executive control systems of the brain. In this context, especially one of this user factors is of special interest, namely the age of the user because there is a tight relationship between the functioning of the prefrontal cortex and the age of the user. Therefore, the development in the phylogeny as well as ontogeny of the prefrontal cortex and the resulting consequence for the experience of Spatial Presence will be discussed in the next subsection.

2.5.2.1 Phylogeny and Ontogeny of the prefrontal cortex

In phylogeny as in ontogeny, the prefrontal cortex is a late-developing region of the neocortex. In the course of evolution the prefrontal cortex grows disproportionately more than other cortical regions. According to Brodmann (1909), the prefrontal cortex constitutes 3.5% of the totality of the cortex in the cat, 12.5% in the dog, 11.5% in the macaque, 17% in the chimpanzee, and 29% in the human (see Figure 2.4). It is a legitimate inference, in any event, that the evolutionary expansion of the prefrontal cortex is closely related to the evolution of cognitive and emotional executive functions (Fuster, 2002).

In accord with the principle that the ontogeny recapitulates phylogeny, the prefrontal cortex and in particular the dorsal part is one of the cortical areas to develop most and last in the course of ontogeny. Neuroimaging and morphometric studies substantiate this general assumption (e.g. Giedd et al., 1999; Giedd, 2004). These studies also indicate that the maturation of grey matter (neurons) has a different time course than the maturation of white matter (myelinated axons). Whereas cortical gray matter follows an inverted U-shape developmental course peaking at about 11 years in girls and 12 years in boys, the volume of prefrontal white matter increases in a roughly linear pattern from childhood to young adults (Giedd, 2004; Giedd et al., 1999; Sowell et al., 1999; Sowell, Thompson, Tessner, & Toga, 2001).

The thickening and thinning of cortical gray matter is thought to reflect changes in the size and complexity of neurons, not a change in the actual number. The increasing size may reflect a process called arborisation in which the cells grow extra branches, twigs, and roots, thereby growing "bushier" and making a greater number of connections to other cells. The decreasing amount of gray matter reflects the process of pruning where connections that are used will survive and flourish, whereas those connections that are not used will wither and die (Giedd, 2004) and therefore probably making recruitment of brain regions subserving executive functions more efficient.

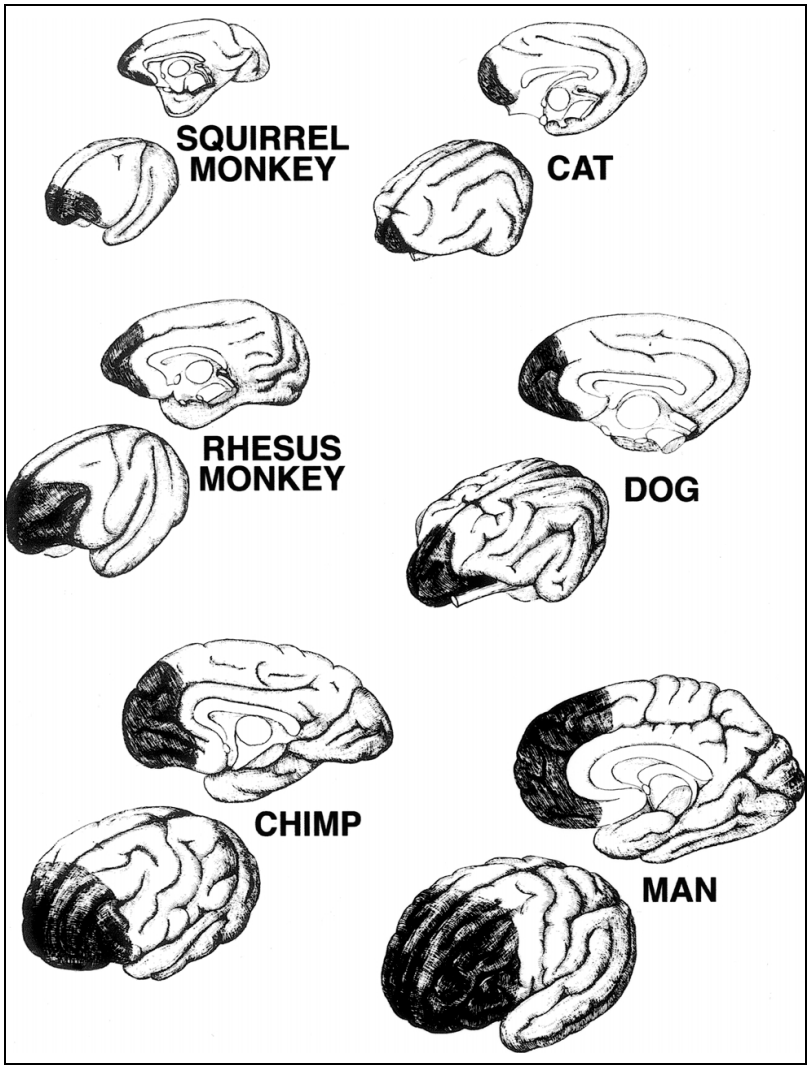

Figure 2.4: Prefrontal cortex (shaded) in 5 animal species and in human (Fuster, 2002).

An increase in white matter (myelination) also improves the functioning of the prefrontal cortex. Myelination is the result of oligodendrocytes wrapping neuronal axons in a fatty sheath that speeds up transportation between neurons – up to 100 times the speed of unmyelinated neurons. It is reasonable to infer that the development of the prefrontal network underlies the developmental of highly integrative cognitive and emotional functions, such as weighting consequences of decisions, prioritizing, and strategizing. Neuroimaging studies

substantiate this assumption (Segalowitz & Davies, 2004; Pujol et al., 2004; Aicardi, 1998). For example, Pujol et al. (2004) investigated 100 children with developmental delay and 50 normally developing age-matched control children using magnetic resonance imaging to measure the volume of myelinated white matter. They found that patients indeed showed a significant reduction in the relative content of the myelinated white matter and this reduction was equivalent to a 3.2 year myelination delay.

In context of Spatial Presence, what is the consequence of this late development of the prefrontal cortex? I suggest that the non-matured prefrontal lobe resulting in reduced executive control functions, including error detection, monitoring, and cognitive evaluation of the virtual reality, leads to an enhanced Spatial Presence experience in children compared to adolescents or adults. This hypothesis is further strengthened by the well known fact that young children experience strong emotions when watching comic movies, reading books and playing computer games (Luna et al., 2001; Ridderinkhof & Vandermolen, 1995; Bjorklund & Harnishfeger, 1990). Moreover, a recent psychometrical study (Schaik, Turnbull, Wersch, & Drummond, 2004) demonstrated that age was indeed negatively related with the Spatial Presence experience in a virtual reality world.

2.5.3 Emotional structures

As already discussed in the Chapter 2.4, Meehan (2001) postulates that physiological Presence means that a user is "responding physiologically to the mediated environment in a manner consistent with human response to similar real situations". Accordingly, if Presence is the extent to which behaviour in virtual reality reflects behaviour in real life circumstances, then of course one would expect high Presence to be associated with the set of emotions that would have been observed in similar real life circumstances. For example, if the virtual reality environment is an everyday, unspectacular situation, high Presence experience should obviously not be associated with strong emotional reactions and therefore I would also not expect strong activation in emotional brain structures. In contrast, if the content of the virtual reality is an arousing, fascinating environment (e.g. a roller coaster ride), I would expect strong emotional reactions and consequently strong activations in emotional brain structures along with psychophysiological reactions of the body. As discussed in Chapter 1.4, emotional reactions are tightly coupled with psychophysiological reactions of the body (see for example Damasio et al., 2000; Craig, 2002). Or in other words, strong somatic and visceral reactions of the body enhance the emotional experience by activation of brain areas involved in mapping and/or regulating of these body states (e.g. insula and somatosensory cortex). Consequently, I

would expect increased activations of these brain areas in an arousing and emotional virtual reality environment.

Furthermore, I would expect a different brain activation pattern in a negative virtual reality world (e.g. a virtual reality exposure therapy for phobic patients) compared to a positive virtual reality environment (e.g. a roller coaster ride, provided of course that the subjects are not afraid of roller coaster riding). In a positive virtual reality environment, one would probably be able to observe an activation increase in the reward centre of the brain, and in particular in the nucleus accumbens which is part of the basal ganglia (e.g. Breiter et al., 1997; Pagnoni et al., 2002). In contrast, fearful virtual reality environments should show strong activations in the amygdala (e.g. Mineka et al., 2002; Ohman et al., 2001). However, recent theories of amygdala functioning have proposed (based on neuroimaging studies) a broader role of the amygdala in emotion processing. For example, Davis and Whalen (2001) suggest for the amygdala a more general role for vigilance or for processing salience, or attributes that make stimuli meaningful.

Taken together, in an emotional and arousing virtual reality world, I would expect strong activation in brain areas involved in emotion processing and mapping of the body states, including for example the amygdala, the nucleus accumbens and the insula (please see Chapter 1 for a detailed discussion of brain structures involved in emotion processing). Furthermore, the pattern of brain activation is different in positive and negative environments, although the exact distinction of brain structures involved in positive and negative emotional reactions is still a matter of current research.

3 Methods: Functional magnetic resonance imaging (fMRI) and electroencephalography (EEG)

In this chapter, the two brain imaging methods used in the studies of this dissertation will be discussed briefly. For a detailed description of these two methods and other brain imaging methods, I want to refer to an excellent current text book by Jäncke (2005).

Functional magnetic resonance imaging (fMRI) provides images of the brain function containing information on metabolism and blood perfusion. Therefore, this method measures the neuronal electrical activity only indirectly with low temporal, but with very high spatial resolution. For instance, in a fundamental study by Logothetis (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001), it was shown that the time course of the fMRI haemodynamic response was roughly a low pass filtered (i.e., low time resolution in the range of seconds) version of the electric neuronal activity. In contrast, electroencephalogram (EEG) measures the neuronal electrical activity directly with an excellent time resolution (in the range of milliseconds), but low spatial resolution. However, new localisation methods (LORETA, see Chapter 3.2.4.2) have markedly improved the spatial resolution of EEG in cortical structures (EEG can not measure subcortical structures). Nevertheless, the spatial resolution of fMRI is still essentially better, namely in the range of millimetres, whereas the spatial resolution of EEG in combination with LORETA is only in the range of a few centimetres. To achieve a good temporal and spatial resolution, both methods should therefore be combined either simultaneously (technically very difficult, but possible, see Chapter 3.2.3) or at different times as conducted in this dissertation.

3.1 Functional magnetic resonance imaging

Functional brain mapping with magnetic imaging (MRI) is a rapidly growing field that has emerged only recently. The goal of fMRI is to map the spatiotemporal distribution of neuronal activity during specific sensory, cognitive or emotional states. By monitoring haemodynamic changes, fMRI indirectly localizes brain functions. Most techniques use the blood oxygenation level dependent (BOLD) contrast in order to investigate what areas of the brain are responsible for specific e.g. cognitive and perceptual processing. The BOLD contrast is based on the differing magnetic properties of oxygenated (diamagnetic) and deoxygenated (paramagnetic) blood. These differences in magnetic susceptibility lead to small, but detectable changes in susceptibility-weighted MR image intensity.

The subsequent sections discuss the BOLD effect, the preprocessing of fMRI data and commonly used statistical methods for analyzing fMRI data.

3.1.1 The blood-oxygen-level-dependent (BOLD) signal

The fundamental signal for blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) comes from hydrogen atoms, which are abundant in the water molecules in the brain. In the presence of a magnetic field, these hydrogen atoms absorb energy that is applied at a characteristic radio frequency (about 64 MHz for a standard, clinical 1.5-Tesla MRI scanner). After this step of applying radio-frequency excitation, the hydrogen atoms emit energy at the same radio frequency until they gradually return to their equilibrium state. The MRI scanner measures the sum total of the emitted radio-frequency energy. The measured radio-frequency signal decays over time, owing to various factors, including the presence of inhomogeneities in the magnetic field. Greater inhomogeneities results in decreased image intensity, because each hydrogen atom experiences a slightly different magnetic field strength, and after a short time has passed (commonly called T2*), their radio-frequency emissions cancel one another out. BOLD fMRI techniques are designed to measure primarily changes in the inhomogeneity of the magnetic field, within each small

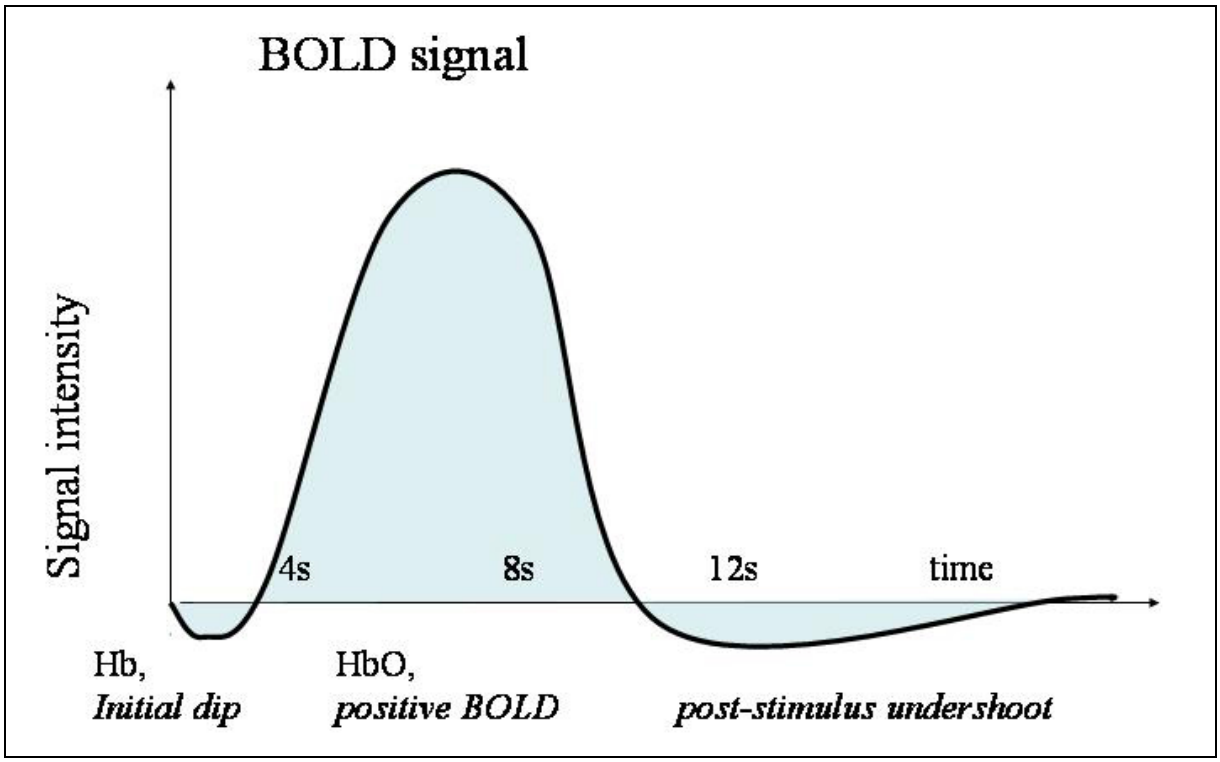

Figure 3.1: Depicted are the three phases of the BOLD response (initial dip, positive BOLD response with maximal BOLD increase at about 4-6 s after stimulation and post-stimulus undershoot; Jäncke, 2005).

volume tissue, that result from changes in blood oxygenation. Deoxy- and oxyhaemoglobin have different magnetic properties; deoxyhaemoglobin is paramagnetic and therefore introduces an inhomogeneity into the nearby magnetic field, whereas oxyhaemoglobin is weakly diamagnetic and has little effect on the magnetic field. Hence, an increase in the concentration of deoxyhaemoglobin would cause a decrease in image intensity, and a decrease in deoxyhaemoglobin would cause an increase in image intensity.

The emerging model of the haemodynamic responses posits that there are three phases of the BOLD fMRI response to a transient increase in neuronal activity (see Figure 3.1): an initial, small decrease in image intensity below baseline (during the initial period of oxygen consumption), followed by a large increase above baseline (an oversupply of oxygenated blood), and then by a decrease back to below baseline again (after the oversupply of oxygenated blood has diminished, it still takes some time for the blood volume to return to baseline). The image intensity increase is approximately 1%-5% for a typical cortical activation task (for an excellent review about the Bold effect please see, Heeger & Ress, 2002).

3.1.2 Preprocessing of fMRI data

The purpose of preprocessing in fMRI is to correct for non-task related variability in experimental data. These approaches are usually performed without any consideration for the experimental design and therefore are called preprocessing. The preprocessing steps seek to remove, rather than model data variability. One important term in fMRI analysis language is the *signal-to-noise-ratio* (SNR), which is the quotient between task-related variability and non-task-related variability. The goal of the preprocessing is to remove as much non-task-related variability as possible in order to obtain a high SNR value. The sensitivity of an fMRI analysis is determined by the amount of residual noise (non-task related variability) in the image series.

The following sections describe four basic steps of preprocessing (although the number of steps depends on the applied experimental design). A number of tools and software programs are available for preprocessing and analysis, such as SPM (http://www.fil.ion.ucl.ac.uk/spm) and Brain Voyager (http://www.brainvoyager.com). For a detailed description of preprocessing using the software program SPM see Friston et al. (1997). The different analysis steps for fMRI data are illustrated in Figure 3.2.

3.1.2.1 Motion correction

Changes in signal intensity over time, from any one voxel, can arise from head motion and this represents a serious confound, particularly in fMRI studies. Despite restraints on head movement, co-operative subjects still show displacements of up several millimetres (Turner, Howseman, Rees, & Josephs, 1997). In addition, there are movements related to physiological factors, such as cardiac and pulmonary parameters. Motion correction algorithms (called realignment) implemented in SPM can correct such artefacts. Realignment involves (1) estimating the 6 parameters of an affine 'rigid-body' transformation that minimizes the [sum of squared] differences between each successive scan and a reference scan (usually the first or the average of all scans in the time series) and (2) applying the transformation by re-sampling the data using tri-linear, sinc or spline interpolation (Friston, Williams, Howard, Frackowiak, & Turner, 1996).

However, motion correction has several limitations, including artefact-related limitations, which can result in a loss of data around the edges of the image volume. Distortions in fMRI images can also pose a problem because distortions may be dependent upon position in field, rather than position in the head. Therefore the rigid body model does not model these types of distortions.

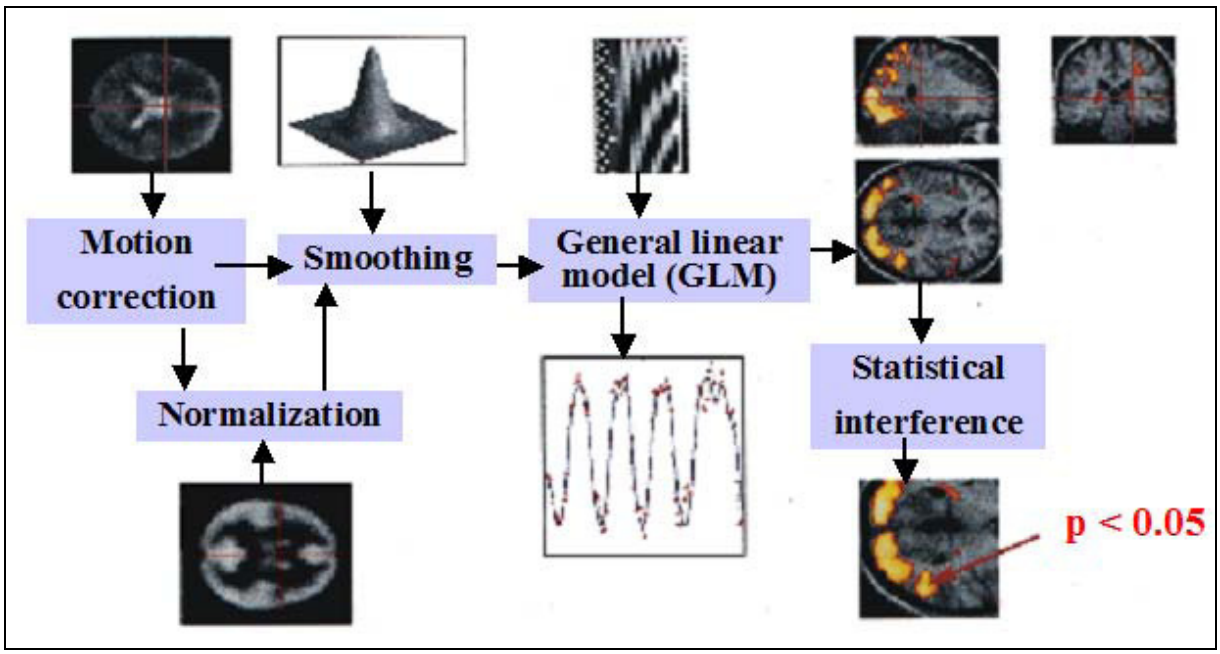

Figure 3.2: Analysis steps for fMRI data (modified from Franckowiak et al. 1997)

3.1.2.2 Coregistration

In order to coregister the anatomical and functional images, the software program in SPM requires three steps. First, it uses simultaneous affine registrations between each image and a

template image of the same modality (functional or anatomical). Next, SPM separates the images into white and gray matter (segmentation). Finally, white and gray matter partitions acquired during step two are simultaneously registered via the sum of squared difference.

The fMRI literature is ambiguous as to whether functional and anatomical images should be coregistered. Coregistration may improve normalization and allow activation on anatomical images to be displayed. It also permits comparison across modalities in an individual's brain. Nevertheless, possible disadvantages of coregistration exist. For example, coregistration may severely distort functional data and may diminish correspondence between functional and anatomical images.

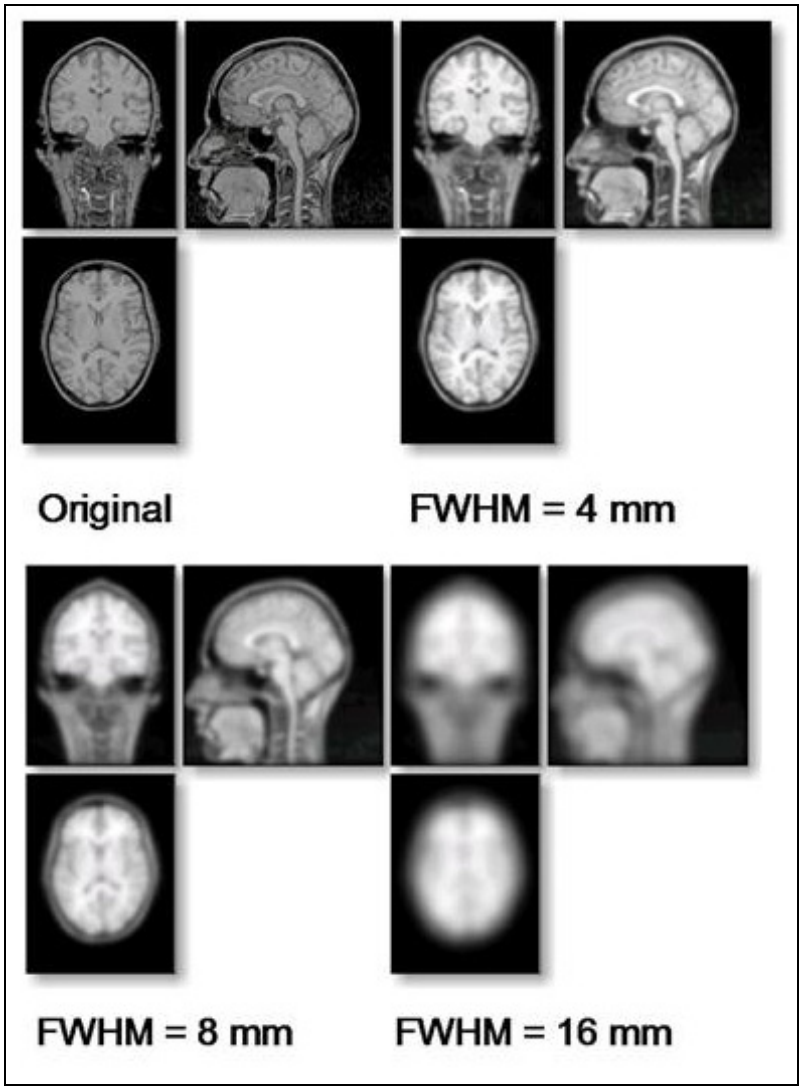

Figure 3.3: Results of different Gaussian smoothing kernel. The figure depicts that an increase of the smoothing parameter leads to reduced spatial resolution (Jäncke, 2005).

3.1.2.3 Normalization

This preprocessing step spatially (stereotactically) normalizes images into a standardized space, which is defined by some ideal model or template image. It can thus be described as an intersubject averaging method. The software program SPM conforms the Montreal Neurological Institute (MNI) space (a combination of many MRI scans on normal controls;

all right-handed subjects) and approximates that of the space described in Talairach and Tournoux's atlas (1988). Generally, these algorithms work by minimizing the sum of squares differences between the acquired images and the template (for automated algorithms see e.g. Ashburner & Friston, 1999). One major advantage of the normalization is that it allows the generalization of results to a larger population, thereby enabling averaging across subjects and improving comparisons with other studies. Normalization also provides coordinate space to report the results. One disadvantage of normalization can be cited in its potential to reduce the spatial resolution resulting from differences in interindividual brain organization and thus may reduce the activation strength by averaging subjects.

3.1.2.4 Spatial Smoothing

Spatial smoothing convolves images with an isotropic Gaussian kernel [defined by its full width at half maximum (FWHM)] to potentially increase SNR, to compensate for residual between-subject variability after normalization, and to approximate a random field for statistical purposes (see multiple comparisons below). Issues such as reduced spatial resolution, which relate to smoothing, are discussed in detail in Friston et al. (2000). Figure 3.3 depicts the results of different smoothing kernel.

3.1.3 Statistical analysis of fMRI data

3.1.3.1 General Linear Model (GLM)

A brief review of the literature may give the impression that there are numerous ways to analyze PET or fMRI time-series with a diversity of statistical and conceptual approaches. This is not the case. With very few exceptions, every analysis is a variant of the General Linear Model (GLM). The GLM is an equation $Y = X\beta + \varepsilon$ that expresses the observed response variable Y in terms of a linear combination of explanatory variables X plus a well behaved error term (Friston et al., 1995). Typically, these GLM approaches result in a statistical parametric map. In order to obtain these parametric maps, each of these approaches entails comparable successive steps.

First, the response (signal) has to be modelled at each voxel in the brain by a GLM. For example, the signal in many experiments is simply modelled by a box-car function convolved with a hemodynamic response function. The box-car function is composed of activation periods and rest periods (see Figure 3.4) and the hemodynamic response function takes into account that the BOLD response reaches the maximum 4-6 seconds after begin of the stimulation (see Chapter 3.1.1).

After modelling, a hypothesis regarding the model's parameters will be tested. The observed statistic map will then be represented at a given level (threshold) according to the point of

distribution of the statistics (uncorrected level) or the field distribution of the statistics (corrected levels for local maxima). A correction to the significance of the t-statistics is suggested, which account for the multiple comparisons in the image (see multiple comparisons below). Afterwards, the statistical parametric map can be visualized showing e.g. the t-value for each single voxel with a corresponding color on an image of the brain. Overall, these methods are voxel-by-voxel hypothesis testing approaches, which reliably identify regions showing a significant effect of interest (e.g. increased activation in the amygdala in the emotional condition compared to the neutral condition).

The GLM model used can refer to a single subject, one group of subjects or multiple groups of subjects, which can represent different subjects (e.g. children or adolescents) or the same subjects (e.g. prior to a cognitive behavioural therapy versus after the therapy). The modelling part is univariate and thus separated for each voxel and usually each subject as well. For a simple t-test, the GLM is also utilized in order to account for covariates as well as temporal

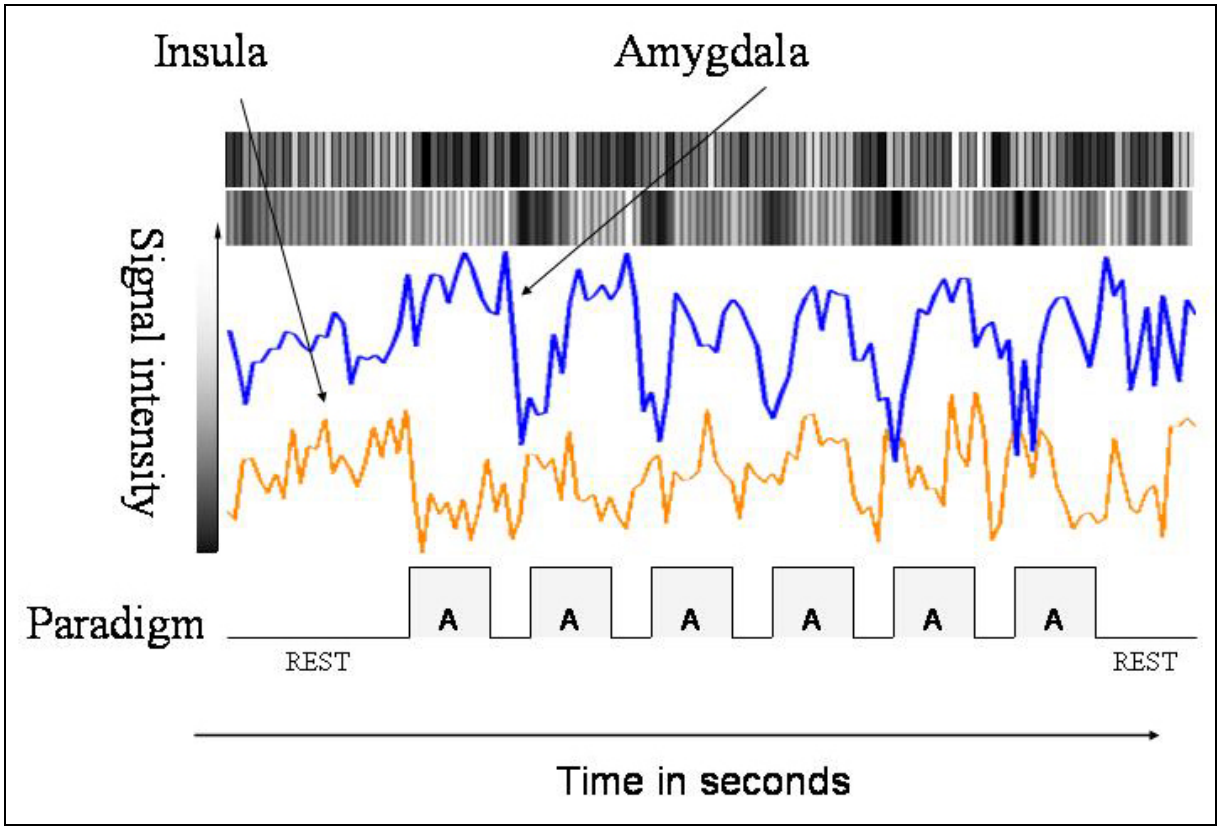

Figure 3.4: Depicted is the time-series of a voxel in the amygdala and insula during the duration of an experiment. A box-car function with activation (e.g. fear pictures) and rest periods (e.g. neutral pictures) is modelled using the GLM approach. Whereas signal intensity of the voxel in the amygdala can be explained by the modelled box-car function (i.e. the voxel shows in the activation period a signal intensity increase and in the rest period a signal intensity decrease), the signal intensity of the voxel in the insula does not follow the modelled box-car function (modified from Jäncke, 2005).

autocorrelation. Multi-subject fMRI experiments can also be performed using a GLM framework with different forms depending on the approach taken, e.g. fixed or random subject analysis. Fixed-effects model uses data from all subjects to construct a statistical test. This method allows interference to the analyzed subject sample only. A random-effects model accounts for inter-subject variance in analyses and therefore, permits interference to population from which subjects are drawn, which is essential for group comparisons.

3.1.3.2 Multiple comparison

Most statistics packages for functional imaging data create statistical parametric maps (see above), which have a value for a certain statistics (e.g. t-statistics) at each voxel in the brain. These results from the statistical test performed voxel-wise between states (experimental tasks) within one subject or over a number of subjects. One major problem arises, however, if more than one test is made, the collective alpha value is greater than the single test alpha (overall Type I error increases). One option is to adjust the alpha value of the individual tests in order to maintain an overall alpha value at an acceptable level (controls overall for Type I error; known as Bonferroni correction). However, conventional multiple comparison methods (e.g. Bonferroni) may overcompensate resulting in very strict significance values for even small data sets.

This problem might be explained by the fact that this approach is not appropriate for correlated data. If data set contains correlated data points, then the effective number of statistical tests may be greatly reduced and most fMRI data has significant correlations. Several approaches are used in fMRI analysis software programs. Some of the primary examples include an approach using the random field theory (Worsley, Andermann, Koulis, MacDonald, & Evans, 1999; Worsley et al., 2002), which provides false positive rate for fMRI data based upon the smoothness of the data, a randomization-based analysis across replications, and applying a small volume correction, e.g. a Region of interest (ROI) analysis (see also next section). A ROI can only be used if an a priori hypothesis has been made.

3.1.3.3 Region of interest (ROI) analysis

Several software programs (MRIcro, BrainVoyager, SPM) include the method of drawing and analyzing Region of Interest (ROI), which can complement a voxel based whole brain analysis. Moreover, SPM offers the possibility to place spheres or boxes centered on specific coordinates into to the measured brain. Jancke (2005) suggests to use spheres with a radius of 6-8 mm. Finally, a new tool exists called anatomic atlas for automatic labelling (Tzourio-Mazoyer et al., 2002) which provides an anatomical parcellation of the spatially normalized single-subject high-resolution template brain provided by the Montreal Neurological Institute

(MNI). This tool defined 45 anatomical volumes of interest in each hemisphere (for example the amygdala) which can be used in SPM for ROI analysis.

The ROI approach allows direct, unbiased measurement of activity in a predefined anatomical region. Because it does not require correction for the number of comparisons, this hypothesis driven approach has more statistical power. Furthermore, a ROI is not smeared due to inter-subject averaging and improves the ability to identify topographic changes. Nevertheless, it should only be used based on previous assessed, clear identified anatomical or functional regions, which allow a directed hypothesis. Since functional ROIs result from statistical tests, they cannot be used to reduce the number of comparisons.

3.2 Electroencephalogram (EEG)

Electroencephalography is the science of recording and analyzing the electrical activity of the brain. Electrodes (as measuring sensors) are placed on the scalp and are linked to amplifiers. In contrast to fMRI, EEG is an old method for measuring brain activation. Richard Caton (1875), a Liverpool physician and medical school lecturer, discovered electrical brain signals by probing directly on the surface of exposed brains in animals. He published his results in 1875. In 1929, the German psychiatrist Hans Berger published the first paper about the human electroencephalogram, where he described the successful recording of brain electric signals measured on the scalp in humans (Berger, 1929).

In the subsequent sections, the recording of EEG data, the electrophysiological basis of EEG, the meaning of frequency bands in terms of activation or deactivation and two analysis methods of EEG data are discussed (event-related desynchronisation/synchronisation and low resolution brain electromagnetic tomography).

3.2.1 EEG recordings

The most commonly used electrode placement is the so-called 10/20-system (Jasper, 1958). This system recommends electrode placement at fixed distances according to ten or twenty percent distance between distinctive landmarks on a subject's head (nasion, inion, and left and right preauricular points), allowing comparable locations for individual head shapes. Electrodes are placed over all brain regions and are labelled accordingly (F for frontal, C for central, P for parietal, T for temporal, and O for occipital). Midline electrode receive the subscript z, left side electrodes have odd numbers, right side electrodes have even numbers. In this fashion, the "name" of an electrode describes its location (e.g. F4: right frontal, Pz: midline parietal). However, it is very important to be aware that the voltage measurements at a certain electrode location (e.g. right frontal) do not necessarily reflect the activity of the

underlying brain area. The reason for this important fact is that electric fields (electrically active neurons) possess orientation and therefore, maximal strength might not be perpendicular to the skull surface (see section 3.2.4.2). The 10/20 system was originally described for 21 electrodes, but it has been extended to accommodate more electrodes. In the studies of this dissertation, a 10/20 system with 30 electrodes was used (depicted in Figure 3.5).

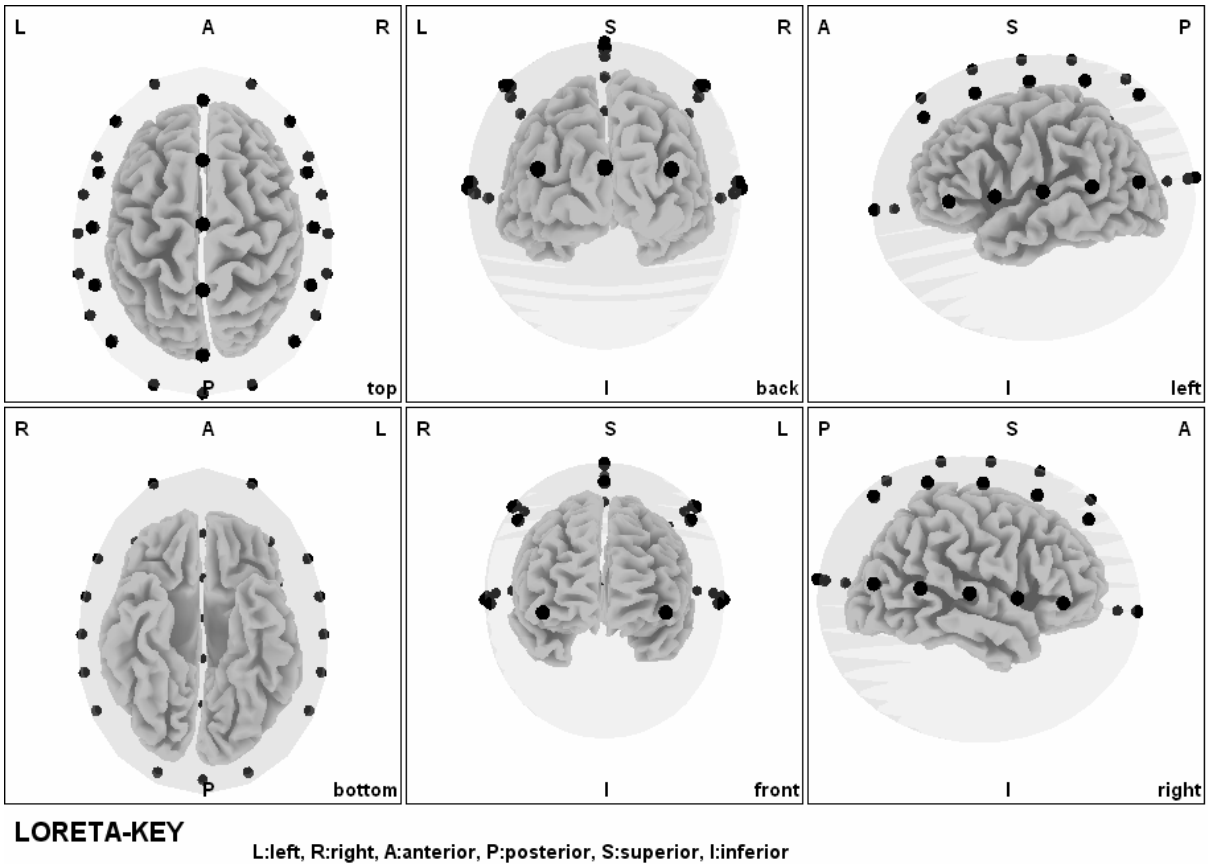

Figure 3.5: Depicted is the electrode montage of 30 electrodes according to the 10/20 system. The electrode positions are indicated by black points on the surface of the scalp. The brain and the electrode positions are depicted in the MNI-space (LORETA-KEY Software).

EEG recordings consist of scalp potential differences between the so-called "active" electrodes and the reference electrode(s). Since there is no electrically inactive location on the human body (Nunez, 1981) against which could be measured all active electrodes, the measured brain voltages cannot be interpreted as absolute potentials. Therefore, the choice of the reference electrode (either the actual physical reference or any recomputed reference) will affect the EEG waveforms. However, it will affect the instantaneous scalp distribution of electric potential (the scalp map) only by a "spatial" offset, a DC level, i.e. an additive to an invariant map landscape. In order the set the "spatial" DC level to zero, the data are transformed into reference-independent values, by recomputing them to the average reference

(Lehmann & Skrandies, 1980). The average reference is computed by subtracting the average value of all electrode values measured at one point in time, from each single electrode value at that point in time. In this way, the DC-offset, i.e. the "spatial" direct current deviating from zero, is subtracted. Thus, if the total electrical charge of the brain is zero, one can eliminate the variation of the electrical potential of the reference that was chosen for recording the EEG. Of course, one has to repeat this procedure for each measurement point during the entire recording.

3.2.2 The electrophysiological basis of EEG

The basis for scalp EEG recordings are the field potentials originating in large neuronal populations. A single neuron does not produce enough electrical current to be measurable on the scalp. The major generators for EEG are post-synaptic potentials, generated by assemblies of cortical neurons, the pyramidal cells. The pyramidal cells are not randomly oriented in the cortical layers but are arranged largely parallel to each other perpendicular to the cortical surface. In order to produce a field strong enough to be recorded at some distance, the neurons must have a certain geometry so that their individual electric fields sum up and do not cancel each other. Another basic condition for the measurement of a remote EEG is instantaneous synchronization of activity, i.e. the simultaneous occurrence of post-synaptic potentials of all pyramidal cells in a cluster. Additionally, the same type of post-synaptic potential, excitatory or inhibitory, advantageously should occur within the same cortical layer, for many pyramidal cells within a cluster. The indirect measurement of the post-synaptic potentials from the scalp with EEG electrodes is possible because the generators are surrounded by conductive media: the cerebrospinal fluid, the meninges, the skull and the scalp.

Two broad classes of activation can be distinguished: (1) "spontaneous" neural activity which constitutes the continuous brain activity, and (2) activity elicited by internal or external stimuli, the "event-related potentials" (ERP) or "evoked potentials" (EP). ERP/EP reflects averaged transient electrical potentials that are time-locked to the repeated presentation of discrete stimuli. Early ERP components reflect the integrity of sensory pathways (e.g. it takes 30 ms for the first five auditory ERP components to reflect activity in the acoustic nerve brainstem nuclei). Later positive (P) or negative (N) ERP components index aspects of preparatory activity (CNV), attention (N100), decision-making (P200), echoic memory (MMM), response activation (N200) and context (P300) of information processing, each within a fraction of a second (Gordon, 1999). Averaging of between 20 and 100 trials is usually sufficient to obtain a reasonable signal-to-noise ratio for ERPs. But it is clear that averaging of more trials will increase signal-to-noise ratio.

In the two EEG studies of this dissertation, no discrete stimuli (Spatial Presence study) or not enough stimuli (Emotion study) were available to obtain ERP's. Therefore, the analysis of the EEG data was conducted using spontaneous neural activity transformed in different frequency bands. The discussion in the next section will therefore focus on the spontaneous EEG and the meaning of the different frequency bands.

3.2.3 Frequency band and brain activation

Even since surface recordings for electrical brain activity were introduced as electroencephalography by Hans Berger, researchers have tried to understand the functional significance of different spontaneous EEG patterns and in particular rhythms (Berger, 1929). Its amplitude ranges between about 5 to 100 micro Volts and its wave frequency conventionally covers a range between 0.5 and 40 Hz. In this dissertation, I distinguish 6 frequency bands according to Kubicki et al.(1979): Delta (1-3 Hz), Theta (4-7 Hz), Alpha (8-12 Hz or 8-13 Hz), Beta1 (13-18 Hz), Beta2 (19-21 Hz), Beta 3 (22-30 Hz). The meaning of these bands in terms of activation and deactivation will be discussed in the next few sections.

3.2.3.1 Delta and Theta

Lowest frequencies, called Delta, range form 1-3 Hz, followed by Theta ranging form 4-7 Hz. These slow frequencies are traditionally assumed to be associated with functional inhibition. In healthy adults, these low frequencies dominate the EEG during sleep. On the other hand, Theta activity is also observed under the condition of focused attention as the so-called frontal midline Theta activity (e.g. Asada, Fukuda, Tsunoda, Yamaguchi, & Tonoike, 1999; Ishii et al., 1999). Some authors (Aftanas & Golocheikine, 2002; Hebert & Lehmann, 1977; Kjaer et al., 2002) found an increase of Theta during meditation compared with a no-mediation condition. Furthermore, Theta oscillations have been implicated in spatial navigation in animals and have been linked in the encoding and retrieval of spatial information in the hippocampus of rodents (O'Keefe & Recce, 1993; Skaggs, McNaughton, Wilson, & Barnes, 1996). Recent human studies using EEG, magnetoencephalography (MEG) or subdurally recorded Theta activity from epileptic patients confirmed the findings from these animal studies (Bischof & Boulanger, 2003; Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999). For example, De Araujo et al.(2001) found a strong increase in Theta activity in temporal regions for virtual maze navigation, but not for either mental calculations or passive viewing of maze navigation, supporting the conclusion that Theta activity is closely tied to spatial navigation.

However, a general, unspecific increase of slow wave activity in adults can be a sign of pathological processes, e.g. vascular diseases or tumours of the central nervous system,

inflammation, dementia, head trauma, intoxication or coma. Moreover, slow waves have a particular relation to ontogenesis: during maturation and development, the dominant EEG frequency in an awake individual increases, from predominant Delta-Theta of the newborn to predominating Alpha in most young adults to predominance of faster activity in the healthy elderly (Klimesch, 1999).

3.2.3.2 Alpha

The human Alpha rhythm is defined as oscillations in electric potential within the 8- to 12-Hz or 8- to 13-Hz range. Some scientist (e.g. Klimesch, 1999) further divide the Alpha rhythm in an Alpha1 band (8-10 Hz) and an Alpha2 band (10-12 Hz). The Alpha oscillation is normally recorded as sinusoidal waves with larger amplitudes over posterior regions, present in roughly 95% of healthy adults. In awake subjects one finds Alpha activity in a state of relaxation, especially when the subjects are seated with closed eyes. In this situation, as soon as the eyes are opened, Alpha activity disappears (so-called Alpha blocking or desynchronisation). The same phenomenon occurs when subjects start to concentrate on mental task (e.g. mental arithmetic), conduct attentional and semantic memory tasks (for a review see Klimesch, 1999). Alpha desynchronisation is a consequence of endogenous or exogenous processes, by task or by stimulation.

Recent studies which implemented continuous and simultaneous EEG/fMRI or EEG/PET strongly confirmed these classical findings. For example Laufs et al. (2003a) demonstrated a strong negative correlation of parietal and frontal cortical activity with Alpha power between 8-12 Hz, i.e. increased BOLD response was associated with decreased Alpha-power at all measured thirty-two electrodes (see Figure 3.6). Goldman et al. (2002) used a region of interest approach to correlate Alpha activity with BOLD responses and found that increased Alpha (8-12 Hz) power was correlated with decreased MRI signal in multiple brain regions of occipital, superior temporal, inferior frontal and cingulate cortex. However, this study and a study by Sadato et al. (1998) also found in a few brain regions positive correlations of Alpha power with brain activation measured with PET or fMRI, including the thalamus and the insula. In contrast, Larson (1998) found in a combined EEG/PET study that an average EEG Alpha power (8-13 Hz) across 28 electrodes was robustly inversely correlated with glucose metabolic activity in the thalamus known to be an important source of afferent projections that modulate cortical Alpha rhythms. While at first, these studies seem contradictory, they actually may highlight different thalamic contributions. Because of the low temporal resolution of the PET method used in the study by Larson (FDG-PET: 30 min for an acquisition of an image), their results may point to trait-like properties of Alpha generation

across subjects. On the other hand, the fMRI study of Goldman (few seconds for the acquisition of an image) or the other PET study of Sadato which used another, faster PET method (^{15}O-PET: 90 s for the acquisition of an image) instead reflect Alpha modulation on an individual level, and thus may highlight the role of the thalamus in moment-to-moment wave generation.

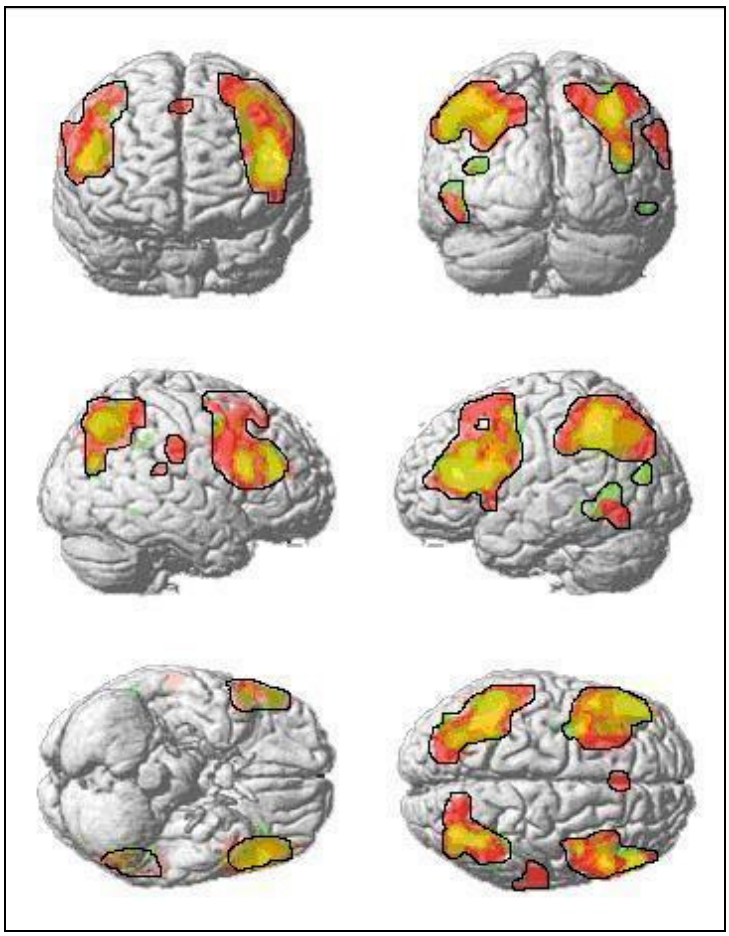

Figure 3.6: Brain areas activated when Alpha power (8-12 Hz) is decreased. Superimposed on a surface rendered T1-weighted anatomical template brain provided by the Montreal Neurological Institute (Laufs et al., 2003a).

3.2.3.3 Beta

In a state of active wakefulness, Beta is the leading frequency band. Beta activity reflects functional excitation and intense mental activity, and is therefore exactly the opposite of the Alpha frequency, i.e. Beta and in particular the high Beta bands (Beta2 and Beta3) are positively correlated with activity. In a recent combined EEG/PET study (Oakes et al., 2004), in which a 3D localisation methods was used to calculate the intracortical distribution of electrical activity (LORETA, see Chapter 3.2.4.2), it was found that with increasing EEG frequency, there was an increase in the number of positively correlated voxels, whereas the lower Alpha band (8.5-10 Hz) was associated with the highest number of negative correlations.

Taken together, these studies indicate that activations in the lower bands (Delta, Theta, but in particular Alpha) are normally negatively correlated with activity, whereas activations in the Beta bands are positively correlated with activity. However, there seem to be some exceptions. In a few brain regions both the Alpha band (in the insula and thalamus) and in particular the Theta band (in temporal regions of the brain) show positive correlations with activity.

3.2.4 Analysis of the EEG data

Two different main approaches are generally used to analyze EEG data. One of these approaches analyses the EEG data at different electrode positions on the scalp (e.g. event-related desynchronisation and synchronisation). However, as stated above, the electrical fields measured at particular electrode sites are too inaccurate to infer the exact underlying intracerebral cortical activations. Therefore, other approaches have been used to more precisely localize the activated brain structures. I focus in the subsequent discussion mainly on the localisation approach used in this dissertation, called low resolution brain electromagnetic tomography (LORETA), but I also discuss shortly the drawbacks of another widely used approach, called Dipole modelling.

3.2.4.1 Event-related desynchronisation and synchronisation

Pfurtscheller and Aranibar (1977) introduced nearly 30 years ago a new method to calculate change in the power of frequency bands between a reference and an activation period, called event-related desynchronisation (ERD) and event-related synchronisation (ERS).

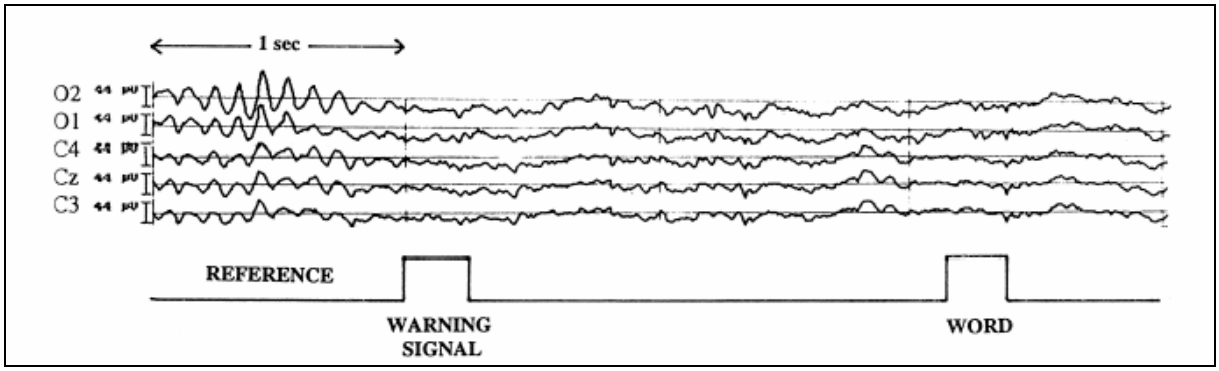

Figure 3.7: Typical example of an EEG epoch, showing the basic principle of Alpha desynchronisation. During the first second of the epoch, which is called reference interval, the subjects show pronounced rhythmic Alpha activity. Subjects run through many trials and thus, the anticipation of the warning signal already causes Alpha to desynchronize even before the warning signal actually appears (Klimesch, 1999).

A typical example of an EEG epoch which is used for measuring ERD is shown in Figure 3.7 (Klimesch, 1999). The subjects' task was to read a visually presented word and to make a

semantic judgement by responding "yes" to a word denoting a living and "no" to a word denoting a non-living object. Before a word appeared a warning signal is presented. Subjects had to judge a total of 96 words. The basic principle for measuring ERD is that Alpha shows a typical phasic change over the time course of trial. After a response, the subject relaxes and awaits the presentation of the next stimulus. This state of relaxed but alert wakefulness is reflected by a pronounced Alpha activity during the reference interval which precedes the trial. Even before the warning stimulus appears the Alpha rhythm becomes suppressed, because the subject anticipates the beginning of the next trial. The Alpha rhythm stays suppressed during the whole duration of the cognitive trial.

The measurement of ERD and ERS is done in several steps (Klimesch, 1999). First, the EEG is band pass filtered within defined frequency bands, the filtered data are squared and then averaged over the number of epochs. Third, band power changes are expressed as the percentage of a decrease or increase in band power during a test (or activation) as compared to a reference (or control) interval by using the following simple formula:

$$\text{ERD} = \left(\frac{(\text{band power reference} - \text{band power test})}{(\text{band power reference})} \right) \times 100$$

Note that desynchronisation (ERD) is reflected by positive values, whereas event-related synchronisation (ERS) is reflected by negative values (Pfurtscheller, 1992; Pfurtscheller, Stancak, Jr., & Neuper, 1996). Importantly, in terms of cortical activation and deactivation the meaning of ERD and ERS values depends on the specific frequency bands. For example, as seen above, Alpha power is in most brain regions negatively correlated with activity (Laufs et al., 2003a), therefore ERD means cortical activation (less Alpha in the test period) and ERS means cortical deactivation (more Alpha power in the test period). In contrast, higher Beta bands are in most brain areas positively correlated with activity (Oakes et al., 2004), therefore ERD in the Beta band means cortical deactivation (less Beta power in the test period), whereas ERS means cortical activation (more Beta in the test period).

3.2.4.2 Low resolution brain electromagnetic tomography (LORETA)

There is no straightforward way to estimate the three-dimensional (3D) distribution of electric neuronal activity from a two dimensional distribution of neuronal electrical activity measured at the electrodes on the scalp. Therefore, several attempts have been made to overcome this problem, called the inverse problem. It is worth emphasizing that behind each particular

solution to the inverse problem, there is some underlying assumption about properties of the generator distribution. For example the first published attempt in EEG source localisation used the dipole model more then 30 years ago (Lehmann, Kavanagh, & Fender, 1969; Henderson, Butler, & Glass, 1975; Kavanagh, Darcey, Lehmann, & Fender, 1978). This long-established method has two major drawbacks. First, this method assumes that, at a given moment in time, all the electrically active neurons are contained within a few square millimetres of cortex. Under certain experimental conditions, this assumptions constitutes a reasonable approximation of reality (e.g. the first components of the brain stem auditory evoked potential, Scherg & Von Cramon, 1985). However, the dipole model breaks down when extended cortical areas are active, as occurs during spontaneous EEG and during cognitive and emotional tasks. Moreover, and even more problematic, an assumption of the numbers of activated dipoles must be made which of course is especially difficult for higher order cognitive and emotional functions, where one hardly knows before hand the exact number of such dipoles or neuronal generators in the brain (Pascual-Marqui, 1999).

In contrast to the dipole method, the method used in this dissertation needs no assumption about the numbers of dipoles and does not assume that the neuronal electrical activity is contained within a few square millimetres of cortex. This method is called low resolution brain electromagnetic tomography (LORETA, Pascual-Marqui, Michel, & Lehmann, 1994; Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002) and solves the inverse problem based on the assumption that smoothest of possible activity distributions is the most plausible one. This assumption is supported by electrophysiology, where neighboring neuronal populations show highly correlated activity (Silva, Amitai, & Connors, 1991). Thus, LORETA results in solutions where neighboring voxels have maximally similar activity. Regardless of the electrophysiological validity of the smoothness constraint, LORETA is capable of correct, although blurred ("low resolution") 3D localization as demonstrated in simulation work as well as in empirical validations (Esslen et al., 2004; Pascual-Marqui et al., 1999; Pascual-Marqui et al., 2002). To compute the intracortical distribution of the electrical activity from the surface EEG data, LORETA computes current density at each voxel in the solution space as the linear, weighted sum of the scalp electric potentials.

The utilized version of LORETA employs a three-shell spherical head model registered to the Talairach human brain atlas (Talairach & Tournoux, 1988) available as digitized MRI from the Brain Imaging Center, Montreal Neurologic Institute. The registration between spherical and Talairach head geometry uses the realistic EEG electrode coordinates reported by Towle et al. (1993). The LORETA solution space is restricted to the cortical gray matter and

hippocampus in the Talairach atlas as defined by the corresponding digitized Probability Atlas available from the Brain Imaging Center, Montreal Neurologic Institute. A total of 2394 voxels at 7 mm spatial resolution are produced under neuroanatomical constraint.

The statistical non-parametric mapping (SnPM) method is used for the statistical analysis of LORETA images (Holmes, Blair, Watson, & Ford, 1996). LORETA images are statistically compared by voxel-by-voxel paired *t*-tests for assessment of differences in localization between conditions (e.g. emotional condition versus neutral condition), thus obtaining t-statistic images. The t-statistic images are then examined to locate regions showing statistically significant effects using a non-parametric approach (Holmes et al., 1996). This approach, using a randomization strategy, determines the critical probability threshold t-values for the observed statistic with corrections for multiple testing. Although this test focuses mainly on maximum signal amplitude for single voxels (single voxel statistics), a second non-parametric analysis assesses the significance of activity based on its spatial extent, obtaining clusters of supra-threshold voxels (cluster statistics).

II. EMPIRICAL PART

4 General aims

Based on the review of the literature in chapters 1-3, the following general aims for the three studies of the empirical part of this dissertation were developed.

General aim 1 (Study A): Assessment of the different global cortical brain activation patterns, psychophysiological body reactions (heart rate, skin conductance responses, respiration and temperature) as well as psychometrical ratings (arousal and valence ratings) of 3 emotions (fear, happiness, sadness) evoked by bimodal (congruent) and unimodal emotional visual and musical stimuli .

General aim 2 (Study B): Assessment of the different cortical and subcortical brain activation patterns of negative emotions (fear and sadness) evoked by bimodal (congruent emotional pictures and musical excerpts) and unimodal stimuli (emotional pictures). Note that in contrast to study A, the spatial resolution of the brain imaging method used in this study is markedly enhanced.

General aim 3 (Study C): Assessment of the neural correlates of Spatial Presence in children and adolescents in an arousing non-interactive virtual reality world depicting different roller coaster rides.

5 Study A: From emotion perception to emotion experience: Emotions evoked by pictures and classical music – an EEG and psychophysiology study

5.1 Introduction

Most of the published neuroimaging papers examining emotional processes have used visual stimuli in order to evoke emotions. In the majority of these studies either the Pictures of Facial Affect by Ekman and Friesen (1976) or the International Affective Picture System (IAPS) by Lang, Bradley and Cuthbert (1995) have been used as stimulus material (e.g. Lee et al., 2004; Esslen et al., 2004; Hariri et al., 2002). This material is composed of stimuli using either facial expressions or sceneries thought to evoke basic emotions (positive or negative). However, it is obvious that real-life emotional experiences mostly rely on the presence of combined stimuli coming from different modalities. For example, music is often used to enhance the emotional impact of movies. Although this enhancing effect of combined presentation of emotional music and visual stimuli is intuitive, modern neuroimaging research has mostly ignored the neurophysiological underpinnings of this enhancement effect. Even the neurophysiological study of emotional experiences associated with the perception of music has been understudied. Emotional appreciation of music is a new research avenue in neuropsychology and neurophysiology (Peretz, 2001). Nevertheless, the results of these few studies are remarkable. It has been shown that music elicits intense emotional responses that activate brain regions thought to be involved in reward/motivation, emotion and arousal, including ventral striatum, thalamus, midbrain, orbitofrontal cortex and the insula (Brown et al., 2004; Blood et al., 2001). These brain structures are known to be active in response to other euphoria-inducing stimuli, such as food, sex, and drugs of abuse (e.g. Small et al., 2001; Breiter et al., 1997).

Although these few studies have demonstrated that music is in fact a powerful elicitor of emotions and especially emotional feelings (Altenmuller, Schurmann, Lim, & Parlitz, 2002; Krumhansl, 1997)**,** there is (to my best knowledge) to date no neuroimaging study which examined the influence of the combined presentation of emotional visual and musical stimuli on the central brain processing. Based on the subjective experience that combined presentation of congruent emotional musical excerpts and visual stimuli might enhance emotional experiences (as compared to the presentation of emotional stimuli from one modality) I designed the present study. In this study, EEG was recorded to measure the

oscillatory brain activity while subjects were listening to emotional musical excerpts of fear, happiness and sadness and while they were viewing at emotionally laden pictures of the same emotional categories. In addition, psychometrical ratings (arousal and valence rating scales) and psychophysiological measures (skin conductance responses, heart rate, respiration and temperature) were collected after and during the experimental conditions, respectively.

5.2 Aims of the study

This study addressed whether the congruent combined presentation of emotional visual and musical stimuli (classical excerpts) compared to the single presentation enhances the general, cortical brain activation, the somatic and visceral body reactions as well as psychometrical arousal and valence ratings of the subjects.

5.3 Hypothesis

I hypothesized that activity in emotional brain structures is increased when the two emotional stimuli modalities are presented in combination compared to the separated presentation of the two modalities. Furthermore, I believe that this increased brain activation is accompanied by increased subjective and psychophysiological arousal and involvement measures because recent findings have strongly supported the idea that the subjective process of feeling emotions is partly grounded in neural maps which represent aspects of the organism's internal state (Damasio et al., 2000; Craig, 2002). Thus, measures from the autonomic nervous system can help to objectively discriminate processes of cognitively evaluating emotions on the one hand or strongly feeling and experiencing emotions on the other hand.

5.4 Methods and Materials

5.4.1 Subjects

24 right-handed (tested with standard handedness tests revealing consistent right-handedness in all subjects) females (mean ± SD age, 26.1 ± 5.3) participated in the experiment, most of them were students of psychology, biology or medicine. Females were chosen because it is known that they show stronger emotional reactions than males. All subjects underwent a physical evaluation to screen out chronic diseases, mental disorders, medication, drug or alcohol abuse. Furthermore, depression, anxiety and alexithymia were assessed by the German versions of the Self-Rating Depression Scale (SDS; Zung, 1965), the State-Trait Anxiety Inventory (STAI; Laux, Glanzmann, Schaffner, & Spielberger, 1981) and the Toronto-Alexithymia Scale (TAS; Taylor, Ryan, & Bagby, 1985). Two of the original 26

subjects had to be excluded because their score in these tests were not within the normal range for the general population. Each subject received 30 Swiss Francs for participating. The study was carried out in accordance with the Declaration of Helsinki principles, approved by the ethics committee of the University of Zurich. All subjects gave written, informed consent and were informed of their right to discontinue participation at any time.

5.4.2 Stimuli and experimental design

The musical stimulus material consisted of excerpts of exactly 70 seconds duration and were taken from the following classical orchestral pieces: 1) Gustav Holst: Mars – *the Bringer of War* from *The Planets, 2*) Samuel Barber, *Adagio for Strings*, 3) Beethoven, *Symphony no.6 (3rd mvt)*. The excerpt by Holst was chosen to evoke fear, the one by Barber was chosen to evoke sadness, and the one by Beethoven was chosen to evoke happiness. Various psychological and psychophysiological experiments have shown that these excerpts are capable of evoking the mentioned three basic emotions (e.g. Krumhansl, 1997; Peretz et al., 1998). In order to avoid startling the participants, the beginning (2 seconds) and the end (2 seconds) of each stimulus were faded in and out.

The visual stimulus material consisted of 48 pictures from the same three emotional categories as the musical stimuli: fear, happiness and sadness. The pictures were taken from the International Affective Picture System (IAPS) or had been collected by the author. All pictures contained humans or human faces, were matched for complexity and rated for emotional content in a pilot experiment by 48 subjects on 9-point scales for valence and arousal. A "9" on the scales indicated that subjects felt very happy and aroused, respectively. The mean ratings (± standard deviations) for the three picture categories were as follows: valence: 2.2 ± 0.76 (fear picture), 3.3 ± 0.69 (sadness picture), 7.8 ± 0.70 (happy picture); arousal: 6.5 ± 0.94 (fear picture), 5.2 ± 0.84 (sadness picture), 6.1 ± 0.81 (happy picture). Fear-inducing pictures depicted for example a man attacking a woman with a knife or a man pointing a pistol to the viewer. The “happiness” pictures showed for example a man holding his smiling baby, laughing children playing on the beach, or athletes in a victory pose. Sadness scenes consisted for example of a crying little boy standing in front of a destroyed house or a couple standing at a gravestone.

The two stimuli modalities (auditory or visual) were presented for 70 seconds either alone or combined. Both the stimuli modalities and the three different emotions were presented in a counterbalanced and pseudo-random order to carefully control for order and habituation effects. Each emotional picture was shown for 4.375 seconds within a block consisting of 16 pictures of the same emotional category. The digitized pieces of music were played during the

whole duration of the experimental conditions. The subjects were instructed to place themselves into the same mood as expressed by the presented emotional stimuli (similar mood induction methods were used by Schneider, Gur, Gur, & Muenz, 1994; Kimbrell et al., 1999; Esslen et al., 2004). The pictures were presented on a 17-inch computer screen and the design was programmed using the presentation software called "Presentation" (Neurobehavioral Systems, Version 0.70, 2003). Subjects were seated at 1.15 meter distance from the screen with their head comfortably positioned in a chin rest.

5.4.3 EEG measures

The electroencephalogram (EEG) was recorded from 30 scalp electrodes using a Brain Vision amplifier system (BrainProducts, Germany). Silver-silver-chloride-electrodes (Ag/AgCl) were used in association with the "Easy Cap System" (International 10-20 system, FMS Falk Minow Services, Herrsching-Breitbrunn, Germany). The electro-oculogram (EOG) was recorded from two additional electrodes placed below the outer canthi of each eye. BrainVision Recorder and Analyzer (BrainProducts, Germany) were used to record (electrode impedance <5 kΩ, 0.5 – 70 Hz, 500 samples/s) and analyze the data.

All recorded EEG-epochs were carefully and individually checked for artefacts by visual inspection. When an artefact occurred in a given channel, data from all channels were removed. The artefact-free EEG material was recomputed to average reference and digitally band passed to 1.5-30 Hz. Artefact-free chunks of data were then extracted through a Hamming window, which reduces spurious spectral power estimates at the beginning and end of each chunk. A fast Fourier transform (FFT) algorithm was applied to all extracted artefact-free epochs of data (each epoch lasted 2.048s). The conditions did not differ in the number of artefact-free epochs used in the analyses (mean = 25.6).

Power density ($\mu V^2/Hz$) was then computed for the Alpha-band (8-13 Hz) because several recent combined EEG/fMRI and EEG/PET papers strongly indicate that power in the Alpha-band is inversely related to activity (Laufs et al., 2003b; Laufs et al., 2003a; Oakes et al., 2004) and is more strongly related to behaviour than power in other frequency bands (Davidson & Hugdahl, 1996). All power density values were log-transformed to normalize the distribution of the data. 16 electrodes were collapsed into 4 electrode clusters: anterior left (F7/F3/FT7/FC3), anterior right (F4/F8/FC4/FT8), posterior left (TP7/CP3/P7/P3) and posterior right (CP4/TP8/P4/P8). The average values across the respective electrode sites were calculated for all 9 conditions and 24 subjects.

5.4.4 Psychophysiological measures

In addition to EEG, heart rate (HR), skin conductance response (SCR), respiration (Resp), and skin temperature (Temp) at the volar surface of the left little finger's distal phalanx (in degrees Celcius) were collected using a commercially available device (PAR-PORT manufactured by Hogrefe Company, Germany). It is well-established that emotion experiences are accompanied by physiological changes that occur automatically without voluntary control. Musical emotion is no exception. On the contrary, music seems to be particularly powerful in eliciting such changes (e.g. Krumhansl, 1997; Khalfa, Isabelle, Jean-Pierre, & Manon, 2002). For SCR recording, electrodes were attached to the thenar and hypothenar areas on the palm of the left hand. Quantitation of SCR's entailed measurement and summation of the SCR amplitude during the 70 seconds experimental period. Log-transformation (log[SCR+1] was used to normalize the SCR amplitude data.

5.4.5 Psychometrical measures

After every experimental condition psychological measures were assessed on a computer-based 5-point scale, ranking from “1 = not at all” to “5 = very strongly”. For this purpose two questionnaires were used: First, three scales of the German version of the Differential Emotion Scale (DES; Izard, Dougherty, Bloxom, & Kotosch, 1974) with three adjectives per scale measuring the three basic emotions of happiness, sadness and fear; and second, three items of the ITC-Sense of Presence Inventory (Lessiter, Freeman, Keogh, & Davidoff, 2001) measuring how much the subjects were involved or engaged in the different emotional experiences.

5.4.6 Statistical analysis

The Alpha-Power-Density values were analyzed in a four-way repeated-measures ANOVA with the following factors: “emotion” (fear, happiness, sadness), “modality” (combined, picture, sound), “region” (anterior, posterior), and “hemisphere” (left, right). For each psychophysiological measurement (SCR, HR, Respiration, Temperature) and the psychometrical involvement scale, two-way repeated-measures ANOVAs were performed with the following factors: “emotion” (fear, happiness, sadness) and “modality” (combined, picture, sound). For three other psychometrical scales (Fear, Sadness and Happiness scales) non-parametric Wilcoxon tests were performed because some of the scales violated the normality assumption necessary to conduct parametric statistical tests. As effect size measure ETA^2 is reported. All statistical analyses were performed using the statistical software package SPSS PC (version 11.5). Results were considered as significant at the level of $p<0.05$.

In case of a significant multivariate effect post hoc paired t-tests were computed using the Bonferroni correction according to Holm (1979).

5.5 Results

5.5.1 Psychometrical and psychophysiological results

The psychometrical results clearly showed that the subjects were able to experience the presented emotions as evidenced by their ratings of the experienced quality of the emotions (see Table 10.1 for mean ratings and standard deviations on page 134). Stimuli chosen to evoke happiness showed the highest scores on the "happiness" scale, and the lowest scores on the "fear" and "sadness" scales, respectively (all significant at $p<0.001$, paired Wilcoxon tests). For those stimuli chosen to evoke fear, subjects reported the highest values on the "fear" scale in every modality, intermediate values on the "sadness" scale and together with the evoked emotion of sadness the lowest values on the "happiness" scale, demonstrating no significant differences between sadness and fear on the "happiness" scale (all at $p<0.001$). Finally, stimuli evoking sadness revealed in every modality the highest values on the "sadness" scale and intermediate values on the "fear" scale (all at $p<0.001$).

More important, as can be inferred from the significant effects presented in Figure 11.1 (a,b,c, please see on page 140), the emotional experience of the presented emotions was most accurate and pronounced in the combined conditions, intermediate in the picture conditions and lowest in the sound conditions. In order to estimate and quantify the distinctiveness of the subjective emotional experiences, ETA^2 was calculated as a mean variability score between each DES-scales separately for each emotion and modality conditions. A high ETA^2 indicates strong differences between the three emotion scales, whereas a low ETA^2 indicates reduced emotional distinctiveness regarding the “happiness”, “sadness” and “fear” scales. Concerning the evoked emotion of happiness, the ETA^2 for all three modalities were very similar (combined: 0.97, picture: 0.95, sound: 0.97) and paired Wilcoxon tests between the three modalities revealed only one significant difference between the combined and the picture conditions, demonstrating a slightly increased rating on the “happiness” scale in the combined condition ($p<0.01$, Figure 11.1 b on page 140). The differences concerning the negative emotional conditions were more extreme (especially for the sound conditions) which is clearly shown by the differences in the ETA^2 measures (combined: 0.93 for the fear condition and 0.95 for the sad condition, picture: 0.89 and 0.88, sound: 0.46 and 0.68). Paired Wilcoxon tests showed that the sound conditions alone evoked less distinctive emotional experiences indicated by increased happiness experiences in both the fear and sad conditions

and reduced fear and sadness experiences in the fear and sad conditions (compared to the combined and picture conditions), respectively (all at $p<0.01$, Figure 11.1 a,c on page 140). Regarding the evoked emotion of sadness, the picture condition alone also showed reduced sadness experience compared to the combined condition ($p<0.01$, Figure 11.1 c on page 140). Finally, both the "sadness" scale in the evoked emotion of fear as well as the "fear" scale in the evoked emotion of sadness were increased in the combined conditions compared to the sound conditions (all at $p<0.01$, Figure 11.1 a,c on page 140). Taken together, the sound conditions showed a reduced emotional clarity compared to the combined and the picture conditions.

On the other hand, both the psychophysiological (SCR, HR, Resp) and the psychometrical involvement measures showed a different pattern. Four two-way repeated-measures ANOVA revealed in all these arousal measurements a highly significant main effect of modality (SCR: $F_{(2,20)} = 19.14$, $p<0.001$, $ETA^2 = 0.657$; HR: $F_{(2,22)} = 20.07$, $p < 0.001$, $ETA^2 = 0.646$; Resp: $F_{(2,21)} = 10.67$, $p<0.01$, $ETA^2 = 0.504$; Involvement scale: $F_{(2,22)} = 13.48$, $p<0.001$, $ETA^2 = 0.551$), demonstrating increased arousal and involvement experiences both subjectively and psychophysiologically in the combined and sound conditions compared to the picture conditions (see Figure 11.1 d on page 140 and 11.2 a,c,d on page 141). Regarding SCR, paired t-tests additionally showed a significant difference between the combined and sound conditions, indicating increased amplitudes in the combined conditions in comparison with the sound conditions. Furthermore, SCR measures showed a significant main effect for emotion (SCR: $F_{(2,20)} = 3.98$, $p = 0.035$, $ETA^2 = 0.285$) which was qualified by reduced SCR's in the happy conditions compared to the negative emotional conditions (Figure 11.2 b on page 141). Regarding respiration, besides the main effect of modality, a significant main effect of emotion ($F_{(2,21)} = 15.19$, $p<0.001$, $ETA^2 = 0.591$) as well as a significant interaction of emotion and modality ($F_{(4,19)} = 5.990$, $p<0.01$, $ETA^2 = 0.558$) was revealed, which clarifies that the increased respiration rate in the combined and sound conditions is only apparent for fear and happiness and could not be found for sadness. Finally, temperature measurement of the left little finger showed a significant main effect of emotion ($F_{(2,22)} = 3.626$, $p = 0.044$, $ETA^2 = 0.248$), revealing decreased temperature in the fear conditions in comparison with the happy conditions. No other significant temperature differences between the three emotions could be observed.

Taken together and most important for this study, the psychometrical and psychophysiological measures of involvement clearly demonstrated higher arousal levels in the combined and sound conditions compared to the picture conditions.

5.5.2 Alpha-Power results

Regarding the brain activation pattern, the four way repeated-measure ANOVA revealed a highly significant main effect of modality ($F_{(2,22)} = 15.55$, $p<0.001$, $ETA^2 = 0.586$), indicating the largest Alpha-Power-Density for the sound conditions, intermediate for the picture conditions, and lowest for the combined presentations of auditory and visual emotional stimuli. A linear trend describes the relationship between the three modalities ($p<0.001$, $ETA^2 = 0.527$; see Figure 11.3 a and 11.4 on page 142). Furthermore, all conditions yielded topographically larger Alpha-Power-Density values over posterior than anterior sites (Region: $F_{(1,23)} = 141.05$, $p < 0.001$, $ETA^2 = 0.860$) and this effect was more pronounced for the sound conditions (Modality*Region: $F_{(2,22)} = 6.724$, $p<0.01$, $ETA^2 = 0.379$). The nearly significant main effects of emotion ($F_{(2,22)} = 3.33$, $p = 0.054$) and hemisphere ($F_{(1,23)} = 3.418$, $p = 0.077$) indicated tendencies for an increased Alpha-Power in the happy conditions compared to the negative emotional conditions and for a greater extent of Alpha-Power in every emotional condition over the left hemisphere, respectively. No other significant effects or tendencies could be observed.

Because the emotional experience was significantly less accurate and pronounced in the sound conditions (see psychometrical results above), an additional four-way repeated-measures ANOVA was conducted excluding the sound modality factor. This analysis showed no additional significant results except the expected significant main effect for emotion ($F_{(2,22)} = 8.96$, $p<0.01$, $ETA^2 = 0.449$), demonstrating an increased Alpha-Power in the happy conditions (combined and picture) compared to the fear and sad conditions (see Figure 11.3 b on page 142).

5.6 Discussion

The results of the psychological ratings clearly showed the subject's ability to experience the presented emotions. More important, the emotional experience of the evoked emotions was most accurate and pronounced in the combined conditions, intermediate in the picture conditions and lowest in the sound conditions. This is substantiated by the clearest difference between the three basic emotions in terms of the emotional ratings. Both the psychological (involvement scale) and the physiological (SCR, HR, Respiration) intensity measurements revealed increased measures in the combined and sound conditions compared to the picture

conditions. Finally, statistical analysis revealed the largest Alpha-Power activity (note that higher Alpha-Power reflects reduced brain activity) for the sound conditions, intermediate for the picture conditions and lowest for the combined presentations of auditory and visual emotional stimuli at all 4 electrode clusters of the brain. Taken together, the combined conditions showed the largest emotional clarity and intensity together with the lowest Alpha-Power-Activity (i.e. stronger cortical activation), indicating the strongest activation over occipital, parietal and frontal, temporal electrode clusters of the brain. Besides the activation increase due to the crossmodal integration of two sensory stimuli (for a discussion of this point, please see limitations section of this study), this strongest activation suggests enhanced activation in a distributed neuronal network for emotion and arousal processing. The results of the picture conditions suggest a markedly reduced emotion experience both subjectively and physiologically – despite of conserved emotion clarity (perception). The sound conditions on the one hand led to reduced emotional clarity and brain activity (largest Alpha-Power = lowest brain activity) but on the other hand to an emotional intensity comparable with the combined conditions.

5.6.1 Comparison between the picture and combined conditions

Modern neuropsychological theories of emotion propose the following processes occurring after the initial presentation of an emotive stimulus (Phillips et al., 2003; for similar models see Scherer, 2000): (1) the appraisal and identification of the emotional significance of the stimulus; (2) the production of a specific affective state, including autonomic, neuroendocrine, and somatomotor responses, as well as conscious emotional feeling; (3) the regulation of the affective state and emotional behaviour. In addition, recent neuroimaging studies (Damasio et al., 2000; Anders, Lotze, Erb, Grodd, & Birbaumer, 2004; for a review see Craig, 2002) have provided strong evidence that cortical activations in brain areas representing somatic and visceral states of the body (e.g. insula, somatosensory association areas) constitute an important part of the basis of emotional feelings. Thus, increased somatic and visceral reactions of the body can be interpreted as strong indicators of increased emotional feelings or experiences. In this study, I found highly significant and consistent increases in somatic (SCR, HR, Resp) and psychometrical involvement measures in the combined compared to the picture conditions, clearly indicating enhanced emotional feelings in the combined conditions of the experiment. Furthermore, this enhanced emotional feeling was associated with increased cortical activation (indexed by reduced Alpha-Power) at anterior and posterior electrode clusters of the brain. The increased cortical activation at posterior clusters (measured at left- and rightsided occipital and parietal electrodes) in the combined conditions

compared to the picture conditions is in line with findings from neuroimaging and electrophysiological studies showing that this part of the cortex is implicated in the modulation of emotion-related arousal (Davidson, Jackson, & Kalin, 2000; Heller, Nitschke, Etienne, & Miller, 1997) and is recruited by emotional visual stimuli (compared to neutral stimuli, Beauregard et al., 1998; Lane et al., 1997; Davidson et al., 2000), in particular, when these stimuli are highly arousing (Lang et al., 1998; Taylor, Liberzon, & Koeppe, 2000). In addition to parietal and occipital structures, functional imaging papers consistently also reported activation in temporal and frontal cortical structures during emotional processing of positive and negative emotional stimuli, including the hippocampus, insula, orbitofrontal cortex, anterior cingulate, dorsolateral and dorsomedial prefrontal cortex (in addition to subcortical structures as the amygdala, thalamus, ventral striatum and brainstem nuclei, for a review see Phillips et al., 2003; Phan et al., 2002). Thus, the increased activity in the combined conditions (indexed by reduced Alpha-Power) in the anterior and posterior electrode clusters of the brain can be interpreted as enhanced emotional processing in several of the aforementioned cortical structures, suggesting increased activity in a distributed emotion and arousal network in the combined compared to the picture conditions. However, future studies are needed to more precisely localize the involved cortical and subcortical structures of this emotional enhancement effect because electrical fields measured at particular electrode sites are too inaccurate to infer the underlying intracerebral cortical activations. Moreover, the increased brain activation in the combined compared to the single modality conditions is at least partly caused by the crossmodal integration of two sensory stimuli coming from different modalities. I discuss this point in more detail in the limitations section of this study (Chapter 5.6.3).

Taken together, the results of this study strongly confirm the idea that music is in fact a powerful elicitor of emotions and can markedly enhance the emotional experience in the context of the presentation of affective pictures. Moreover, this study shows that emotional reactions (e.g. emotional experiences or feelings) are relatively weak if only visual stimuli are used. Therefore, I believe that this stimulation mode will in most cases not evoke emotional feelings (or at least in a markedly reduced way) but rather a more cognitive, less arousing emotional perception process. I hypothesize that this finding could be one of the reasons for the often discrepant findings in emotion research (e.g. experimental results relative to hemispheric lateralization of emotional processing and differential activation during different emotions diverge in multiple ways), indicating that different emotion induction methods lead to different activations of the three emotional processes in the model by Phillips et al. (2003)

mentioned above. I suggest that in particular the production of a specific affective state (including autonomic, neuroendocrine, and somatomotor responses as in process 2 of the described model) varies widely between different induction methods as has been shown in this experiment between the picture and the combined conditions.

5.6.2 Musical emotions: a paradox?

A further interesting finding of this study is the relatively strong Alpha-Power during listening of emotional musical excerpts. Although these stimuli evoked strong emotional reactions (indicated by increased SCR, HR, Resp and psychometrical measures) the cortical activation substantially decreases compared to both the combined and the picture conditions. Whereas the increased Alpha-Power activity (note that higher Power reflects reduced brain activity) in occipital and parietal electrode clusters of the brain can easily be explained by the reduced visual input in this condition (fixation cross versus emotional pictures), the increased Alpha-Power activity in frontal and temporal electrode clusters requires another explanation.

One explanation could be that the neural electrical activity is reduced because the sound stimuli are overall more pleasant as indicated by the valence ratings which showed that the ratings of the negative musical stimuli (sad and fear sound) were significantly less negative compared to both the negative combined and picture conditions. In line with this interpretation, several recent neuroimaging and electrophysiological studies have demonstrated reduced brain activation during positive compared to negative emotional stimuli (Carretie, Mercado, Tapia, & Hinojosa, 2001; Northoff et al., 2000; Schmidt & Trainor, 2001). However, this interpretation can not fully explain the finding of this study because the main effect of modality clearly indicates that musical stimuli irrespective of valence evoked reduced brain activation compared to the combined and picture conditions. Therefore, I favour another explanation. I hypothesize that the dissociation between the involvement measurements and the brain activity (in posterior and anterior electrode clusters of the brain) support the notion that emotional musical excerpts activate an internal mode of brain function. This internal mode is characterized by cognitive and emotional processes revolving around the subject's internal state instead of current external events or circumstances (Gusnard, Akbudak, Shulman, & Raichle, 2001; Raichle et al., 2001). Accordingly, fronto-parietal attention networks (Corbetta & Shulman, 2002) preparing the subject to react adequately to external events or circumstances show diminished activations, leading to reduced cortical brain activation indexed in this study by increased Alpha-Power-Activity.

Evidence for this interpretation comes from a PET study of Blood and Zatorre (2001) which demonstrated that intensely pleasant responses to music correlated positively with activations

almost exclusively in subcortical structures, whereas strong negative correlation were found in the prefrontal and posterior neocortical regions (precuneus/cuneus), clearly indicating that strong and arousing emotional experiences can be evoked without strong activation in cortical brain regions. Accordingly, Damasio (2000) demonstrated during the feeling of self-generated emotions widespread activation decreases in neocortical brain regions, including frontal, temporal, parietal and occipital areas. In contrast, primarily subcortical brain areas were strongly activated along with strong psychophysiological as well as psychometrical arousal measures. Therefore, I believe that these findings indicate that reduced activation in cortical regions and increased psychometrical and psychophysiological arousal measures are not a paradox. I hypothesize that subcortical region, such as for example the amygdala, the striatum and the thalamus are activated in the musical condition of this experiment leading to strong emotional experiences and somatic and visceral body reactions. However, as well-established, EEG can not detect such subcortical brain activation patterns.

5.6.3 Limitations

Due to the lack of a neutral control condition (neutral music doesn't exist, for an explanation see Krumhansl, 1997; Peretz et al., 1998; Cooke, 1959), one could argue that the increased brain activation in the combined condition is simply produced by multimodal cortical networks known to be involved in the integration of simultaneously presented auditory and visual information (Downar, Crawley, Mikulis, & Davis, 2000; Calvert, Hansen, Iversen, & Brammer, 2001; Beauchamp, Lee, Argall, & Martin, 2004). However, I do not think that the modality effects of this study can be fully explained by such neutral crossmodal integration processes. The following reasons speak clearly against such an interpretation. First, and most obvious, the subjects consistently reported an increased emotional involvement along with enhanced somatic reactions of the body in the combined conditions. Second, in addition to the modality specific effects, valence specific effects in physiological measures in good agreement with the literature were found implying that the emotion induction procedure used in this study was successful and that the observed change in the brain activation pattern between the different modalities is influenced by the emotional valence of the stimuli. Regarding brain activations and SCR, I observed in the combined and the picture conditions but not in the sound conditions (note that the sound conditions were characterized by reduced emotional clarity) significant valence specific effects, demonstrating increased emotional brain processing and SCR levels in the negative emotional conditions (sad and fear) and a markedly reduced overall brain activation and SCR level in the positive conditions (e.g. Northoff et al., 2000; Carretie, Hinojosa, Martin-Loeches, Mercado, & Tapia, 2004). In

addition, reduced skin temperature of the left little finger in the fear conditions compared to the happy conditions as well as reduced respiration rates in the sad conditions compared to the happy and fear conditions were found (Krumhansl, 1997; Stemmler, Heldmann, Pauls, & Scherer, 2001), further indicating successful emotion induction in the happy, fear and sad conditions. Nevertheless, I do not question that the activation of the crossmodal integration areas contribute to the observed emotional enhancement effect. Future studies are needed to clearly differentiate between a neutral crossmodal integration process and an emotional enhancement process.

5.7 Conclusion

Summing up, this is the first neurophysiological study demonstrating a strong emotional enhancement effect by simultaneous presentation of congruent emotional pictures and music regarding subjective ratings, peripheral and central physiological measures. Moreover, this study implies that strongest emotional reactions (experience) cannot be evoked by presenting emotional pictures alone (at least in most cases), but only by simultaneous presentation of congruent emotional musical excerpts. Therefore, I believe that this emotion induction method can make an important contribution to an improved understanding of the neural structures involved in emotional feelings and psychiatric disorders as depression and anxiety.

6 Study B: The emotional power of music: How music enhances the feeling of affective pictures – a fMRI study

6.1 Introduction

Music is widely used to enhance the emotional impact of movies. For example, in thrilling horror movies (e.g. Scream) music and sound effect enhance the feeling of fear and anxiety and in movies about aids (e.g. Philadelphia) or holocaust (e.g. Schindler's List) music is normally used to increase the feeling of sadness. For some of the spectator, this congruent visual and auditory experience could become even so emotional that they could no longer bear it and therefore they would turn off the TV, in particular when watching scary movies. Another strategy to reduce the emotional experience to a tolerable level often reported by spectators is simply to turn off the sound of the movie. Surprisingly, this emotional "on-off switch" effect has received little attention in the brain research literature. To my best knowledge, there exists no neuroimaging study which explored the cortical and subcortical underpinnings of this enhancement effect using emotional pictures and musical excerpts. Note that the described EEG study in Chapter 5 could only explore the cortical correlate of this enhancement effect with low spatial resolution (subcortical structures can not be detected using EEG). As discussed in Chapter 3, the electrical fields measured at particular electrode sites are too inaccurate to infer the underlying intracerebral cortical activations.

Although no brain imaging study has ever explored the cortical and subcortical correlates of this enhancement effect using emotional visual and musical stimuli, a few recent studies have impressively demonstrated the emotional power of music. In these studies, musical excerpts alone elicited strong emotional responses that activated brain regions known to be involved in reward/motivation, emotion and arousal, including ventral striatum, thalamus, midbrain, orbitofrontal cortex, the insula and the anterior cingulate cortex (e.g. Blood et al., 2001; Blood et al., 1999; Brown et al., 2004). Moreover, there are a few behavioural and brain activation studies which addressed the question of the integrated perception of emotion regarding voice and face stimuli. Behavioural studies have revealed that congruent crossmodal perception of emotional faces and voices leads to (1) a facilitation in facial emotion recognition (de Gelder et al., 2000) and (2) to enhanced affective judgements of emotional faces (for example, a fearful face is more likely to be perceived as fearful if accompanied by a fearful voice; Massaro et al., 1996). The first study which directly addressed this integration question using fMRI revealed that congruent fearful face-voice pairs compared with incongruent pairs (happy voice + fearful face) elicited increased activation in the amygdala and the fusiform

gyrus (Dolan et al., 2001). In a recent similar study using both single and combined modality conditions, activation in the right extended amygdala was obtained for fearful faces and fearful audio-visual pairs but not if fearful voices were presented alone, thus demonstrating no enhanced brain processing in the amygdala in the combined congruent emotional condition (Pourtois et al., 2005). However, the perception of audio-visual emotions (positive and negative) relative to unimodal conditions was associated with activation in the anterior fusiform gyrus and medial temporal gyrus known to be involved in multisensory integration of neutral and emotional stimuli (Mesulam, 1998; Adolphs et al., 2002).

This is the first neuroimaging study exploring the effect of crossmodal binding of emotional musical excerpts and affective pictures or in other words, I examined for the first time the described emotional "on-off switch" effect using a method to examine the involved cortical as well as subcortical structures with high spatial resolution. Thus, functional magnetic resonance imaging (fMRI) was used to localize the cortical and subcortical structures playing an important role in the proposed emotional enhancement effect. In this fMRI study, fearful, happy and sad pictures of the International Affective Picture System (Lang et al., 1995) were presented in a classical block design either alone or combined with congruent classical musical excerpts known to evoke the same emotional experience as the pictures.

6.2 Aims of the study

The aim of this study is to explore with high spatial resolution the cortical as well as subcortical underpinnings of the proposed emotional enhancement effect.

6.3 Hypothesis

Due to the explorative nature of the study and to increase the statistical power, I focused my interest on two neural systems, proposed in a recent excellent review (Phillips et al., 2003) about the neurobiology of emotion perception: a ventral and a dorsal system (see Chapter 1.1.3). The authors suggest based on recent animal, human lesion, and functional neuroimaging studies that the ventral system, including the amygdala, insula, striatum, thalamus, brainstem nuclei, and ventral regions of the anterior cingulate cortex and prefrontal cortex, is important for the identification of the emotional significance of the stimuli, the production of affective states (including autonomic, neuroendocrine, and somatomotor responses, as well as conscious emotional feeling), and automatic and autonomic regulation of emotional responses. The dorsal system, including the hippocampus and dorsal regions of the anterior cingulate gyrus and prefrontal cortex, is more important for cognitive processes,

including selective attention, planning, and effortful rather than automatic regulation of affective states. I expected that the emotional musical stimuli mainly increase the emotional significance of the visual stimuli and moreover, enhance the conscious emotional feeling and somatic body reactions (as demonstrated in the EEG study discussed in Chapter 5). Therefore, I hypothesized an activation increase in the combined compared to the picture condition mainly in the automatic ventral system of emotion processing. Furthermore, because the subjects had no explicit cognitive task (they only had the instruction to feel to presented emotions), I hypothesized no change in activation between the two conditions or rather an activation decrease in the cognitive dorsal system in the combined condition. However, the medial temporal lobe memory system (including the hippocampus and the parahippocampus) which is part of the dorsal system has been shown to be strongly activated during the encoding phase of highly arousing emotional stimuli. This activation was present although the subjects were not explicitly instructed to memorize the presented stimulus material, indicating that the memory system is automatically activated by emotional stimuli (Dolcos, LaBar, & Cabeza, 2004). Therefore, I would also expect increased activation in the memory system of the brain in the more arousing combined condition of our experiment. In addition to the regions of the dorsal and ventral system of emotion processing, I included, based on the findings by Dolan et al. (2001) and Pourtois et al. (2005) mentioned above, the extrastriate cortex, and in particular the fusiform gyrus and the crossmodal integration areas (the medial temporal gyrus and the temporal pole) in the a priori regions of interest, expecting increased activation in these areas in the combined relative to the picture condition.

6.4 Methods and Materials

6.4.1 Subjects

9 right-handed (tested with standard handedness tests revealing consistent right-handedness in all subjects according to the criterion proposed by Annett, 1970), healthy females (mean ± SD age, 24.78 ± 2.9, range: 21-30) were examined in the study, all of them students at the University of Zurich, Switzerland. Female participants were chosen because previous studies showed that, compared to men, women are more likely to report intense emotional experiences along with stronger physiological reactions of the body (Lang, Greenwald, Bradley, & Hamm, 1993). All subjects underwent a physical evaluation to screen out chronic diseases, mental disorders, medication, and drug or alcohol abuse. Furthermore, depression and anxiety were assessed by the German versions of the Self-Rating Depression Scale (SDS; Zung, 1965) and the State-Trait Anxiety Inventory (STAI; Laux et al., 1981). Four of the

original 13 subjects had to be excluded. Two of them because their score in the STAI and SDS questionnaires were not within the normal range for the general population and the other two because of technical sound problems during the experiment. Each subject received 50 Swiss Francs for the participation. The study was carried out in accordance with the Declaration of Helsinki principles, approved by the ethics committee of the University of Zurich. All subjects gave their written, informed consent and were informed of their right to discontinue participation at any time.

6.4.2 Stimuli

54 fear-, sad-, and happy-inducing pictures were taken from the International Affective Picture System (IAPS) or had been collected by the author (about 70% percent of the pictures were taken from the IAPS). All pictures contained humans or human faces, were matched for complexity and rated for emotional content in a pilot experiment by 48 subjects on 9-point scales for valence and arousal ("9" indicating that the subjects felt very happy and aroused, respectively). The results of the pilot study clearly indicated that the presented stimuli were perceived as highly arousing negative or positive pictures. The mean ratings (± standard deviations) for the three picture categories were as follows: valence: 2.1 ± 0.71 (fear picture), 3.1 ± 0.73 (sadness picture), 7.7 ± 0.70 (happy picture); arousal: 6.8 ± 0.90 (fear picture), 5.5 ± 0.83 (sadness picture), 6.0 ± 0.77 (happy picture). The emotional musical stimuli were taken from classical orchestral pieces and consisted of excerpts of exactly 44 seconds duration. One excerpt of Gustav Holst (*Mars – the Bringer of War* from *The Planets*) was chosen to evoke fear, one excerpt of Samuel Barber (*Adagio for Strings*) was chosen to evoke sadness, and one excerpt of Beethoven (*Symphony no.6*) was chosen to evoke the emotion of happiness. Various psychological and psychophysiological experiments have shown that these excerpts are capable of evoking the mentioned three basic emotions (e.g. Krumhansl, 1997; Peretz et al., 1998). Musical stimuli were presented binaurally through MRI-compatible headphones with an individually adjusted comfortable listening level (between 70 and 80 dB). The visual stimuli were presented via a video projector onto a translucent screen that subjects viewed inside the scanner via mirror. All stimuli were presented under computer control (Presentation, Neurobehavioral systems, version 0.79, 2003). Note that the same stimuli as in the EEG study were presented (see Chapter 5). However, 6 additional pictures were used which explains the slightly different mean ratings of the pilot study (see above).

6.4.3 Study Design

The fMRI measurements were conducted in the context of a classical block-design experiment during which stimulation (ON period) alternated with rest (OFF period). The whole experiment consisted of one run of 18 minutes and 28.8 seconds duration resulting in a total of 504 Scans (TR: 2.2 seconds). During this run, 6 different emotional blocks were repeated two times (3 emotions: fear, happiness, sadness and two modalities: picture or combined) resulting in a total of 12 emotional stimulation periods (6 picture conditions and 6 combined conditions). A block consisted either of 9 different emotional pictures of the same emotional category alone (happy, fear or sad pictures) or combined with the congruent musical excerpt (happy picture together with happy music, fear picture together with fear music, and sad picture together with sad music). The pictures were presented in pseudo-random order for 4.8 seconds with a gap of 100 ms between each picture. The same musical stimuli were presented during the whole emotional condition, but in order to avoid startling the participants, the beginning (2 seconds) and the end (2 seconds) of each stimulus were faded in and out, respectively. Both the visual as well as the musical stimuli were presented twice during the experiment. All visual stimuli were presented with and without music. The musical excerpts were never presented alone. Before every emotional condition, a short instruction screen was presented for 4.4 seconds (2 TR's) which instructed the subjects to place themselves into the same mood as expressed by the presented emotional stimuli (similar mood induction methods were also used by Schneider, Gur et al., 2002; Kimbrell et al., 1999; Esslen et al., 2004). After each experimental condition, subjects gave two affective ratings via button-press on a computer-based 5-point scale (valence and involvement ratings, ranking from "1 = negative or weak" to "5 = positive or strong"). The involvement rating measured how strong the subjects were involved or engaged in the different emotional experiences. Every of these two affective questions were presented for 11 seconds resulting in 22 seconds for both questions (10 TR's). Finally, a fixation cross was presented for 22 seconds (10 TR's) between every emotional conditions.

Because some emotion papers have shown strong emotional habituation effects (e.g. Stark et al., 2004), I carefully controlled for these habituation and order effects. Thus, half of the subjects (n = 5) first experienced the picture conditions and afterwards the combined conditions whereas the other half of the subjects (n = 4) first experienced the combined conditions and afterwards the picture conditions. The presentation of three picture conditions of every emotional category (fear, sad and happy) was always followed by the presentation of

three combined conditions of every emotional category or vice versa. The different emotions were further presented in a counterbalanced and pseudo-random order.

At the end of the experiment, the following two questions regarding the noisy scanner environment had to be answered separately for each emotion on a 5-point scale, ranking from "1 = I agree not at all" to "5 = I agree very strongly": "Despite the noise scanner environment (1) I was able to apprehend the musical excerpts and (2) I was able to recognize the emotional tune of the musical excerpts". Furthermore, the subjects had to rate their emotional intensity experience on a 5-point scale (separately for each emotion), where "3" indicated that the emotional experience in the combined conditions was equal intense as in the picture conditions, "1" and "2" indicated that the picture conditions were more intense than the combined conditions and finally, where "4" and "5" indicated that the emotional experience in the combined conditions was stronger than in the picture conditions.

6.4.4 Data Acquisition

The Experiment was conducted on a 3 Tesla Philips Intera whole body MR Scanner (Philips Medical Systems, Best, The Netherlads) equipped with an 8-channel Philips SENSE head coil. Structural image acquisition consisted of 160 T_1–weighted sagittal images (1mm slice thickness). For functional imaging, a total of 504 volumes were obtained using a SENSitivity Encoded (SENSE, Pruessmann, Weiger, Scheidegger, & Boesiger, 1999) T_2 *-weigthed echo-planar imaging sequence using an acceleration factor of 2.0. 36 axial slices were acquired covering the whole brain with a slice thickness of 3mm; no inter-slice gap; interleaved acquisition; TR = 2200 ms; TE = 35ms; flip angle = 77°, field of view = 220mm; matrix size = 80 * 80. The orientation of the axial slices was parallel to the AC-PC line.

6.4.5 General image analysis

For the preprocessing and statistical analyses, the statistical parametric mapping software package (SPM99, Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Version 6.5) was used. For analysis, all images were realigned to the first volume, corrected for motion artefacts and normalized ($4mm^3$) into standard stereotaxic space (template provided by the Montreal Neurological Institute), and smoothed using a 12 mm full-width-at-half-maximum Gaussian kernel. The six experimental conditions, fear, sadness and happiness (picture and combined), were modelled with a box-car function convolved with a hemodynamic response function in the General Linear Model of SPM. A band-pass filter, which was composed of a discrete cosine-basis function with a cut-off period of 264 seconds for the high-pass filter and a canonical hemodynamic response function for the low-pass filter,

was applied. In order to increase signal to noise ratio, global intensity changes were minimized by scaling each image to the grand mean.

6.4.6 General statistical analysis

For the different analyses, different t-contrast images were calculated at the individual level (first level). To increase the statistical power due to the small number of repetition of the different conditions (only two per condition), I decided to combine the negative emotional conditions (fear and sadness) for statistical analysis for the following reason. Several recent studies on brain activity have demonstrated that negative and aversive events elicit more prominent emotional responses than do positive or neutral ones (e.g. Carretie et al., 2001; Northoff et al., 2000; Carretie et al., 2004). Thus, the analysis was focused in this study on the negative emotional conditions and the brain activation pattern of the happy conditions will not be analysed and reported. However, the psychometrical ratings for all 3 emotional categories will be reported. Therefore, 3 different conditions were used in this paper for the analysis of the different brain activation patterns: (1) Combined condition (composed of sad and fearful musical and visual stimuli), (2) Picture condition (composed of sad and fearful visual stimuli), and fixation baseline (fixation cross in the middle of the screen). Accordingly, four t-contrast images at the individual level were calculated: combined versus picture (C>P); picture versus combined (P>C); combined versus fixation (C>F); picture versus fixation (P>F). The resulting contrast images were used for a subsequent second-level analyses.

For the *a priori* regions of interest, I used for these second-level analyses a voxel-wise intensity threshold of $p < 0.005$ (uncorrected for multiple comparison) with a spatial extent threshold of five contiguous voxels. The statistical criterion was selected on the basis of similar criteria used for the examination of a priori regions of interest in other neuroimaging studies employing random-effects statistical models (e.g. Hamann & Mao, 2002). Based on previous studies (Dolan et al., 2001; Pourtois et al., 2005) and the two neural systems for emotion perception proposed by Phillips et al. (2003), the medial temporal lobe system (including the amygdala, the hippocampus and the parahippocampus), the ventral and dorsal prefrontal cortex, the anterior cingulate, the insula, the striatum, the brainstem nuclei, the thalamus, the fusiform gyrus, the medial temporal gyrus and the temporal pole were defined as the regions of interest. Due to the explorative nature of the study, I also applied for regions about which there was no clear a priori hypothesis the same uncorrected threshold of $p < 0.005$ for all hemodynamic related statistical analyses (cluster threshold: 5 voxels). However, findings of the exploratory analysis should be regarded as tentative because of these relatively relaxed criteria.

In addition to the second-level analysis, regions of interest (ROI) analysis for medial temporal lobe structures were conducted. ROIs were marked using an anatomic atlas for automatic labelling of structural brain images normalized into MNI space (Tzourio-Mazoyer et al., 2002) and included: (1) amygdala; (2) hippocampus; (3) parahippocampal gyrus. For each ROI mean T-values were computed for each subject and each condition based on the contrasts combined versus fixation baseline (C>F) and picture versus fixation baseline (P>F). To be sure that the activation in the amygdala is not influenced by the smoothing of neighbouring regions (a rather large smoothing filter for the whole brain analysis was used), unsmoothed data to calculate the ROI analysis were used. Finally, these mean T-values of the ROI analysis were used to correlate the brain activation pattern in the amygdala, the hippocampus and parahippocampus with the psychometrical arousal ratings obtained at the end of the experiment. For this purpose, a mean psychometrical arousal rating was calculated including fear and sad ratings.

Three different strategies were applied to analyze the similarities and differences between the combined and picture conditions. First, the brain regions displaying significant activation during the combined and the picture conditions were descriptively examined for the contrast combined versus fixation (C>F) and picture versus fixation (P>F). Then I analyzed (by means of a second-level model) which of the brain regions showed statistically significant changes in activation between the combined and the picture conditions for the contrasts combined versus picture (C>P) and picture versus combined (P>C). Finally, the differences between combined and picture conditions were explored using a ROI approach which focused specifically on the medial temporal lobe system and in particular the amygdala.

Psychometrical and ROI analyses were performed using the statistical software package SPSS for PC (version 11.5). For the two psychometrical measures (valence and involvement rating scales), two-way repeated-measures ANOVAs were performed with the following factors: “emotion” (fear, happiness, sadness) and “modality” (combined, picture). For every region of interest, a two-way repeated-measure ANOVA was calculated with the following factors: "modality" (combined, picture) and "hemisphere" (left, right). Results were considered significant at the level of $p<0.05$. In case of a significant multivariate effect post hoc paired t-tests were computed using the Bonferroni correction according to Holm (1979). As effect size measure ETA^2 is reported.

6.5 Results

6.5.1 Psychometrical results

Repeated-measures ANOVA regarding the valence scale demonstrated a highly significant main effect of *emotion* ($F_{(2,7)} = 132.6$, $p < 0.001$, $ETA^2 = 0.974$) and a trend for a significant interaction between *emotion* and *modality* ($F_{(2,7)} = 3.6$, $p = 0.083$, $ETA^2 = 0.509$), indicating that the subjects were clearly able to differentiate on a 5-point scale between the negative (fear condition: mean ± SD: 1.3 ± 0.3; sad condition: 1.4 ± 0.6) and positive emotions (happy condition: 4.7 ± 0.4) and more interesting, that the subjects experienced the different emotions more extreme in the combined condition, that is they rated the happy condition more positive and the sad and fear condition more negative when congruent emotional music was simultaneously presented (see Figure 11.5 on page 143). Repeated-measures ANOVA regarding the involvement scale revealed a highly significant main effect of *modality* ($F_{(1,8)} = 11.6$, $p < 0.01$, $ETA^2 = 0.594$) which was qualified by an increased involvement and arousal experience in the combined (mean = 4.32, SD = 0.35) compared to the picture conditions (mean = 3.88, SD = 0.55). In addition, the subjects clearly indicated at the end of the experiment on 5-point scales (separated for each emotion) that, despite of the noisy scanner environment, (1) they were able to apprehend the musical excerpts (fear music: 4.22 ± 0.83; sad music: 4.33 ± 0.9; happy music: 4.33 ± 0.7); and (2) that they were able to recognize the emotional tune of the musical excerpts (fear music: 4.22 ± 1.1; sad music: 4.67 ± 0.5; happy music: 4.56 ± 0.7). Furthermore, all subjects also confirmed at the end of the experiment that they had experienced the combined conditions as more intense than the picture conditions (fear: 4.33 ± 0.7; sad: 4.67 ± 0.7; happy: 4.33 ± 0.8). One sample t-tests revealed that these ratings significantly differed from the value 3 (all $p < 0.001$) which would have been chosen by the subjects if the emotional intensity in the combined conditions would have been equal as the intensity in the picture conditions. Summing up, the psychometrical ratings clearly indicated that the emotional experiences during the combined conditions were significantly increased compared to the picture conditions and that the subjects were able to apprehend and recognize the emotional musical excerpts despite of the noisy scanner environment.

6.5.2 Brain activation data

6.5.2.1 Combined versus fixation (C>F) and picture versus fixation (P>F)

Results for these two contrasts are listed in Tables 10.2 (page 135) and 10.3 (page 136). As expected, both contrasts revealed widespread bilateral haemodynamic responses in the occipital lobe (inferior and middle occipital gyrus, cuneus, fusiform gyrus) and in the bilateral

cerebellum. In both contrasts, activation was also found in the limbic system (parahippocampus and hippocampus), but with the distinction that the activation was more distributed and bilateral in the combined condition. Left amygdala activation, activation in the right precentral gyrus and in the pons as well as expected bilateral activation in the temporal lobe (superior, middle and inferior temporal gyrus) was only observed in the contrast combined versus fixation (C>F). Finally, only the contrast picture versus fixation (P>F) revealed strong haemodynamic responses in the right lateral prefrontal cortex (inferior frontal gyrus) as well as small haemodynamic responses in the left middle frontal gyrus.

6.5.2.2 Combined versus picture (C>P) and picture versus combined (P>C)

Results for these two contrasts are shown in Figure 11.6 (page 144) and 11.7 (page 145) and listed in Table 10.4 (page 137). Contrasting the combined condition with the picture condition (C>P) revealed as expected widespread bilateral activations in the superior and middle temporal gyrus. In addition, this contrast was associated with increased activations in the ventral part of the medial frontal lobe, in the parietal cortex (posterior cingulate/precuneus), in the bilateral fusiform gyrus, in the limbic system (bilateral amygdala, hippocampus and parahippocampus), in the motor system (bilateral cerebellum, right precentral gyrus), in subcortical structures (left nucleus caudatus, right pons) and the left insula.

Contrasting the picture condition with the combined condition (P>C) mainly revealed activations in the dorsal part of the right prefrontal cortex (right inferior frontal gyrus, right middle frontal gyrus, left superior frontal gyrus). No further significant activations were observed despite of the relatively relaxed statistical threshold of $p < 0.005$ (uncorrected).

6.5.3 Regions of interest analysis

According to the main hypothesis, regions of interest analysis were conducted using unsmoothed data to examine the activation in the medial temporal lobe system, including the amygdala, the hippocampus and the parahippocampus. Two-way repeated measures ANOVA's regarding the extracted mean t-values of the contrast images combined versus fixation (C>F) and picture versus fixation (P>F) revealed for all three examined structures of the medial temporal lobe system a significant main effect of *modality* (Amygdala: $F_{(1,8)} = 15.6$, $p < 0.01$, $ETA^2 = 0.661$; Hippocampus: $F_{(1,8)} = 7.8$, $p < 0.05$, $ETA^2 = 0.494$; Parahippocampus: $F_{(1,8)} = 10.5$, $p < 0.05$, $ETA^2 = 0.567$). This main effect clearly indicated increased haemodynamic responses bilateral in the amygdala, the hippocampus and the parahippocampus in the combined condition in comparison with the picture condition (see Figure 11.8 on page 146). One sample t-tests further confirmed these findings showing that only the combined condition led to an activation increase in these structures which was

significantly different from zero (all $p < 0.05$). No main effect of hemisphere and no interaction effect of hemisphere*modality was observed. Similar ROI results were obtained using the smoothed data (12 mm) of the whole brain analysis (not presented here).

6.5.4 Correlation analysis

Because the regions of interest analysis revealed strong bilateral activation in the amygdala, the parahippocampus and hippocampus in the combined compared to the picture condition, the correlation analysis was conducted using the mean activation of both hemispheres. A strong positive correlation was found between the amygdala and the arousal ratings obtained at the end of the experiment ($r=0.73$, $p=0.024$, 2-tailed, see Figure 11.9 on page 147), strongly indicating that subjects having experienced the combined condition as more intense also showed increased activations in the amygdala. No correlation between the arousal ratings and the hemodynamic responses in the hippocampus and parahippocampus were found (all $p>0.35$).

6.6 Discussion

The observed psychometrical results and brain activation pattern confirmed the hypothesis of enhanced emotional processing in the combined condition compared to the picture condition (note that only the negative emotional conditions were explored). Subjects reported that the emotional experience was more intense during the combined conditions along with increased activation in most of the brain areas proposed to compose the automatic ventral system of emotion perception (Phillips et al., 2003), including bilateral amgygdala, ventral frontal cortex, left striatum, left insula, and brainstem nuclei (right pons). Furthermore, I also observed in the combined condition compared to the picture condition a stronger activation in the medial temporal lobe memory system (including the hippocampus and parahippocampus) which is part of the more cognitive dorsal system for emotion perception. Finally, I could confirm the hypothesis of enhanced brain activation in the combined condition in extrastriate visual processing areas (fusiform gyrus) and in brain areas known to be involved in neutral and emotional visual-auditory integration processes (right temporal pole, bilateral medial temporal gyrus; Mesulam, 1998). Apart from these hypothesized structures, I found in the combined condition an activation increase in brain areas involved in emotion and memory (posterior cingulate/precuneus, Maddock, Garrett, & Buonocore, 2003) as well as in motor control (bilateral cerebellum, right precentral gyrus). Summing up, most of the hypothesized brain areas (as expected mainly in the ventral system of emotion perception) showed increased activation in the combined compared to the picture condition.

In contrast, the picture condition (composed only of negative pictures) only showed an activation increase in the more cognitive dorsal system for emotion perception, mainly in the right dorsolateral prefrontal cortex (right inferior frontal gyrus, right middle frontal gyrus) as well as a smaller activation increase in the left superior frontal gyrus. This frontal activation pattern is compatible with current theories of emotional processes (Davidson et al., 1999; Davidson, 2003) suggesting increased left frontal brain processing for approach-related positive emotions and increased right frontal processing for withdrawal-related negative emotions. No other activation increase in the picture condition relative to the combined condition was observed despite of the relatively relaxed statistical threshold of $p < 0.005$ (uncorrected, cluster threshold: 5 voxels).

In the following, I will first discuss the increased activation in the combined condition (C>P) and afterwards the increased activation in the picture condition (P>C).

6.6.1 Discussion of the increased activation in the combined condition (C>P)

6.6.1.1 Activations in auditory cortex and crossmodal integrations areas

As expected, the combined condition revealed haemodynamic responses bilateral in the entire primary and secondary auditory cortex (comprising BA 22, 41, 42) and the activation was more widespread in the right hemisphere, in agreement with studies of passive listening to music of non-musicians (Zatorre et al., 1994; Ohnishi et al., 2001). In addition, bilateral strong activation in the medial temporal gyrus (BA 21) and the right (BA 38) and left temporal polar region (BA 21) were found. The medial temporal gyrus plays a role in multisensory integration (Mesulam, 1998) and brain damage to the temporal polar cortex impairs emotional recognition of both facial and vocal stimuli (Adolphs et al., 2002). In a recent crossmodal study using emotional voices and faces (Pourtois et al., 2005), it was found that the bimodal condition compared to the two unimodal conditions was associated with increased activity in the left medial temporal gyrus for positive voice-face pairs and in the right medial temporal gyrus for negative voice-face pairs. With my study, this lateralisation pattern could not be confirmed for positive and negative emotions because I found bilateral activation in this brain region for the combined condition (composed only of negative stimuli). Nevertheless, the results of this study suggest that the medial temporal gyrus and the temporal pole are not only involved in the crossmodal binding of voice and face stimuli but also in the crossmodal integration of congruent emotional pictures and musical excerpts.

6.6.1.2 Activation in the amygdala

The amygdala is a key structure in emotion processing involved both in the identification of the emotional significance of a stimulus and the production of an affective state (Phillips et al., 2003). I found activation within the amygdala only during the combined condition, but not during the picture condition. Previous studies have reported amygdala activation to a wide variety of emotional stimuli, including fear faces (Morris et al., 1996; Phillips et al., 1997), aversive pictures (Taylor et al., 1998; Simpson et al., 2000), sad (Blair et al., 1999) and happy faces (Breiter et al., 1996; Pessoa et al., 2002), positive pictures (Hamann et al., 1999; Garavan et al., 2001), film excerpts (Aalto et al., 2002; Reiman et al., 1997), as well as positive (laughing) and negative (crying) sound stimuli (Sander et al., 2003; Sander et al., 2001). The finding of an absence of amygdala activation to the picture condition is therefore surprising. However, in a recent meta-analysis of 55 neuroimaging studies Phan et al. (2002) showed that only 50 percent of experiments using visual induction methods activated the amygdala. Furthermore, studies have demonstrated that an increasing intensity of sad (Blair et al., 1999) and fearful (Morris et al., 1996) facial expression is associated with enhanced activity in the amygdala. A recent study complemented these findings by demonstrating that the amygdala activation was dependent on both the intensity and type of displayed emotion, with significant responses to fearful facial expressions and to a lesser degree to happy expressions (Glascher et al., 2004). Therefore, the absence of amygdalar activation in the picture condition as well as the presence of amygdala activation in the combined condition can be explained (at least to a large portion) by differences in arousal levels which are apparently in the picture condition to low to reach the threshold for amygdala activation. This interpretation is further strengthened by an observed strong positive correlation between psychometrical arousal measures and amygdala activation in the combined condition and is in line with current theories of amygdala function postulating for this structure a more general role for vigilance or for processing salience, or attributes that make stimuli meaningful (Davis & Whalen, 2001).

6.6.1.3 Activation in both memory systems

In addition to the increased activation in the amygdala, I observed as expected in the combined relative to the picture condition an increased activity bilateral in the medial temporal lobe memory system supporting "declarative" memory (including the hippocampus and parahippocampus) as well as in the left nucleus caudatus supporting "procedural" memory (for a review of the two memory systems, see Packard, 1999; Devan & White, 1999). Recent evidence strongly support the idea that the amygdala exerts a modulatory influence on

the hippocampus-dependent as well as caudate-dependent memory systems (for a review, see Packard & Cahill, 2001; McGaugh, 2004). For example, memory for emotionally arousing material is not enhanced in human subjects with bilateral and selective lesions of the amygdala, as it is in normal subjects (Adolphs, Cahill, Schul, & Babinsky, 1997; Cahill, Babinsky, Markowitsch, & McGaugh, 1995). Furthermore, various recent fMRI studies using incidental learning paradigms (i.e. the subjects were not aware during the encoding phase of the subsequent memory tasks) demonstrated enhanced activity in the amygdala and the medial temporal lobe memory system for emotional arousing scenes during the encoding phase of the experiment as well as correlations between subsequent episodic memory and levels of amygdala activation during encoding of negative and positive stimuli (Dolcos et al., 2004; Canli, Zhao, Brewer, Gabrieli, & Cahill, 2000; Hamann et al., 1999). These studies clearly indicate that the medial temporal lobe memory system can be activated in a rather automatic way, modulated by strong activation of the amygdala as has been observed in the combined condition in this study. Therefore, I suggest to adapt the model by Phillips et al. (2003) by including the medial temporal lobe system not only in the cognitive dorsal system but also in the automatic ventral system for emotion processing as a transition zone between emotion and cognition.

6.6.1.4 Activation in extrastriate visual processing areas

Another interesting finding of this study (never reported before in neuroimaging papers) revealed that emotional musical stimuli can enhance the activity in visual processing areas (fusiform gyrus). Thus, this study confirms and extends the findings of studies demonstrating that crossmodal integration processes of congruent faces and voices increase the activity in the fusiform gyrus (Pourtois et al., 2005; Dolan et al., 2001). I suggest that this enhanced processing in the bilateral fusiform gyrus is evoked by markedly increased arousal levels in the combined relative to the picture condition. In line with this interpretation, it has been shown that maximally intense expressions of emotions compared with neutral or modestly intense expressions were associated with enhanced activity in extrastriate visual processing area, and in particular the fusiform gyrus (Glascher et al., 2004; Surguladze et al., 2003; Lang et al., 1998; Taylor et al., 2000). Comparable with the influence of the amygdala on the medial temporal lobe memory system, it has been postulated in previous studies (e.g. Morris et al., 1998; Rotshtein, Malach, Hadar, Graif, & Hendler, 2001) that this enhanced activity in visual cortical areas is modulated by the amygdala. Consistent with this proposal, as reported above, I found in the combined but not in the picture condition bilateral activation of the

amygdala. Therefore, the increased activation in the fusiform gyrus in this study could indeed be modulated by the amygdala.

6.6.1.5 Further activations

Besides the increased activation of the amygdala, the medial temporal lobe memory system and the fusiform gyrus in the combined condition, further structures showed increased activation in the combined compared to the picture condition, including hypothesized structures of the ventral system for emotion processing as the ventral medial frontal gyrus, the left insula and brainstem nuclei (right pons) as well as not hypothesized structures as the posterior cingulate/precuneus, bilateral cerebellum and right precentral gyrus. The activations of these structures are completely in line with the proposal of enhanced emotion processing in the combined compared to the picture condition. For example, ventral frontal regions (including the orbitofrontal cortex and the ventromedial frontal cortex) have been associated with the representation of the emotionally salient states of reward and punishment (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001; Rolls, 2004; Rolls, 2000), and decision-making tasks requiring the manipulation of emotionally salient information (Bechara, Damasio, Tranel, & Anderson, 1998).

The insula, another structure showing increased activity in the combined condition, has been implicated in the mapping of body related sensations, including temperature, pain, proprioception, and viscera (Craig, 2002) and consistent with this mapping hypothesis, insula activations were mainly found during aversive emotional stimulation that also evoked visceral/somatic sensation, including disgust (Phillips et al., 1997), sadness (George et al., 1996), fear conditioning (Buchel et al., 1999), and processing of fearful faces (Anderson et al., 2003a). Moreover and in line with the finding of increased insula activation in the combined condition, Morris et al. (1998) showed that the insula was responsive to increasing intensity of fear.

The nuclei of the pons have been implicated in negative emotions of sadness and anger (Damasio et al., 2000) and especially acoustic startle responses to negative stimuli (Yeomans & Frankland, 1995). These nuclei receive projections from the cingulate cortex and the insula, and send projections to the cerebellum. Therefore, Damasio (2000) hypothesized that these projections guide the cerebellum in modulating and coordinating varied emotional action programs. Consistently, I also found bilateral activation of the cerebellum and the precentral gyrus in line with other emotion studies which have reported cerebellar activations both for negative and positive emotional stimuli (e.g. Lane et al., 1997; Taylor et al., 2000; Damasio et al., 2000; Reiman et al., 1997; Taylor, Phan, Decker, & Liberzon, 2003).

Finally, I found in the combined compared to the picture condition stronger activations of the posterior cingulate/precuneus. This brain area is involved in various functions including episodic memory (Maddock et al., 2003), spatial attention (Mesulam, Nobre, Kim, Parrish, & Gitelman, 2001) and emotional stimulus processing (Damasio et al., 2000; Esslen et al., 2004; Maddock & Buonocore, 1997) and is heavily connected with frontal and temporal cortical areas (Morris, Pandya, & Petrides, 1999; Allison, Puce, & McCarthy, 2000). Therefore, it is suggested that this region mediates interactions of emotional and memory-related processes (Maddock et al., 2003), two processes which were strongly activated in the combined condition relative to the picture condition.

6.6.2 Discussion of the increased activation in the picture condition (P>C)

6.6.2.1 Activation in the prefrontal cortex

Most interesting, a clear functional and structural dissociation was observed between the combined and picture condition. Whereas the combined condition demonstrated additional or increased activation in most structures of the ventral system for emotion processing, the picture condition only showed one strong activation increase in the cognitive dorsal system, mainly in the right dorsolateral prefrontal cortex (BA 44/45). The dorsolateral prefrontal cortex is known to be involved in effortful regulation of attention, affective states, and autonomic responses (Phillips et al., 2003). Moreover, studies specifically observing the influence of different task instructions observed a similar functional and structural dissociation between more implicit (passive viewing) and more explicit emotion processing tasks (emotion-labeling task). Whereas the more implicit emotional processing tasks were associated with increased activity in the amygdala-hippocampal region, the more explicit emotion processing tasks were associated with increased activity in the prefrontal cortex, and in particular in the dorsolateral prefrontal cortex (BA 44/45; Hariri, Bookheimer, & Mazziotta, 2000; Nakamura et al., 1999). In addition, consistent with these findings, Phan et al. (2002) demonstrated in a recent meta-analysis of emotional neuroimaging studies that experiments using an implicit emotion processing tasks were approximately 10 to 15 percent more numerous in demonstrating activation of subcortical regions (including the amygdala and the hippocampus), whereas emotional studies using a more explicit cognitive task were 15 to 20 percent more numerous in demonstrating activation in the dorsal anterior cingulate and prefrontal cortex.

In this study, the task instructions was not varied; the subjects had to follow in the combined as well as in the picture condition the same instruction, namely to place themselves into the same mood as expressed by the presented emotional stimuli. However, the distinctive brain

activation patterns and subjective ratings clearly indicate that carrying out the instruction during the combined condition must have been much easier and more automatic than during the picture condition. I hypothesize that the musical excerpts in the combined condition helped the subjects in a rather automatic and implicit way to feel the presented emotional experiences, whereas in the picture condition the subjects were cognitively evaluating the emotional stimuli or were even effortful and explicitly trying to up-regulate their affective states (as is known with moderate success), leading to activation of the dorsolateral prefrontal cortex. These findings strongly suggest functional and structural dissociation between processes of cognitively evaluating emotions on the one hand and strongly feeling and experiencing emotions on the other hand. I postulate that different induction methods either activate more the *cognitive mode* or the *feeling mode* of emotion processing. Accordingly, these findings can give an explanation for the often discrepant findings in emotion research regarding for example amygdala activation or lateralisation patterns.

6.6.3 Limitations

The finding of increased activation in the combined condition in most structures known to be involved in various emotional processes is striking (for excellent reviews see, Phillips et al., 2003; Phan et al., 2002). However, I am aware that this study has a major limitation. Other than the study of Pourtois et al. (2005), no single musical condition was included in this study. Therefore, one cannot not exclude that the activation pattern in the combined condition could also have been produced by the musical stimuli alone. In fact, most of the structures observed in the combined condition are reported in the literature to be activated by musical and sound stimuli (vocal and non-vocal) alone, including the orbitofrontal gyrus, the amygdala, the insula, the striatum, the cerebellum, the hippocampus and the parahippocampus (Blood et al., 2001; Brown et al., 2004; Sander et al., 2001; Phillips et al., 1998; Blood et al., 1999; Zatorre et al., 1994). Whereas most of these studies only showed activation in a few structures of the dorsal and ventral system for emotion perception, mainly one study (Blood et al., 2001) exploring the neural mechanism underlying intensely pleasant emotional responses to music using positron emissions tomography (PET) found a similar complex pattern of activation in this emotion network. However, no activation increase in the amygdala and the medial temporal lobe memory system was observed in this study, despite of high arousal levels. Interestingly, to date, only vocal (Phillips et al., 1998) and non-vocal sound stimuli (Sander et al., 2003) were reported to activate the amygdala. Similar to positive and negative visual stimuli which preferentially activated the amygdala (Phan et al., 2002), sound stimuli are important to evaluate changes in the environment, whereas musical stimuli alone have no

direct evolutionary connection to the external world and therefore presumably activate a more internal mode of brain function (Gusnard et al., 2001; Raichle et al., 2001). Consistent with these findings, it is postulated that the amygdala may be more responsible for processing of externally-cued perceptual emotional stimuli (Reiman et al., 1997; Teasdale et al., 1999).
Nevertheless, despite of the interesting finding that no study to date has ever reported activation in the amygdala triggered by musical stimuli, I cannot rule out that the observed activation pattern in the combined condition could have been produced (at least partly) by musical stimuli alone. However, I want to emphasize the fact that the main goal of this study was not to explore specifically the effect of multimodal and unimodal brain processing, but rather to compare two different emotion induction methods which were never compared using neuroimaging methods. Therefore, this is the first neuroimaging study showing how musical stimuli can markedly enhance the emotional experience evoked by affective picture, namely by stronger or additional activation of most structures known to be involved in emotion perception and experience. Or in other words, although highly arousing emotional pictures of the International Affective Picture System were used, emotional musical excerpts still had the power to significantly increase the activation in most structures of the proposed emotional network for identification of the emotional significance of a stimulus and production of affective states. This is all the more remarkable because, in spite of using ear-phones and ear-plugs, the noisy scanner environment never can be completely suppressed. However, this noisy scanner environment might be the reason that two structures involved in emotion processing and arousal, including the thalamus (Anders et al., 2004) and the ventral part of the anterior cingulate (Elliott, Friston, & Dolan, 2000; Esslen et al., 2004), showed no activation increase in the combined condition in this study, whereas the study of Blood et al. (2001) using similar emotional musical excerpts in the silent PET environment was able to observe an activation increase in these structures of the ventral system for emotion perception. Thus, I conclude that not surprisingly, the emotional power of music is attenuated in the noisy fMRI compared to a silent PET environment, yet still impressively effective demonstrated in this study by highly distinctive psychometrical ratings and brain activation patterns between the combined and the picture condition.

6.7 Conclusion

Summing up, this is the first neuroimaging study showing that classical music can strongly enhance the emotional processing of highly arousing affective pictures by increasing the activation in most structures of the ventral system for emotion processing, including the

amygdala, the ventral medial frontal gyrus, the striatum, the insula, the brainstem, and the medial temporal lobe memory system (including the hippocampus and parahippocampus, proposed by the author of this dissertation to be also part of the ventral system). Moreover, this study also showed that congruent emotional musical stimuli can increase the activity in extrastriate visual processing areas, an area which have never before shown to be activated by musical stimuli alone. Finally, a clear structural und functional dissociation was found between the combined and the picture condition. Whereas the combined condition was associated with increased activation in a large and distributed network involved in emotion processing, the picture condition only showed one strong activation increase in the dorsolateral prefrontal cortex which is part of the cognitive dorsal system for emotion processing. I argue that these findings indicate that emotional pictures evoke a more cognitive emotional perception process, whereas combined presentations of congruent visual and musical emotional stimuli rather automatically evoke (strong) emotional feelings and experiences.

7 Study C: The neural correlate of Spatial Presence in an arousing and non-interactive virtual reality world – an EEG and psychophysiology study

7.1 Introduction

Spatial Presence which is a specific variant of the Presence concept is a relatively unusual concept for psychologists and neuroscientists. Spatial Presence is considered as „a sense of being there“ which „occurs when part or all of a person's perception fails to accurately acknowledge the role of technology that makes it appear that s/he is in a physical location and environment different from her/his actual location and environment in the physical world“ (Schubert et al., 2001). Typically, Spatial Presence occurs in virtual situations created by the perception of spatial cues of the media content, not by cues of the real physical world. According to this view, television, radio, virtual reality technology (VR) and even books should be able to produce Spatial Presence in different ways.

However, although much research has been devoted to the study of Spatial Presence and Presence using psychometrical (Huang & Alessi, 1999; Robillard et al., 2003; Larsson, Vastfjall, & Kleiner, 2001; Flanagan, McAnally, Martin, Meehan, & Oldfield, 1998; Slater, Steed, McCarthy, & Maringelli, 1998; Mania & Chalmers, 2001; Vastfjall, 2003) or psychophysiological methods (e.g. Meehan et al., 2002; Meehan, 2001; Wiederhold et al., 2002b; Laarni, Ravaja, & Saari, 2004) only few studies have focussed on the neurophysiological and neuroanatomical underpinnings of Spatial Presence. Most studies in the neuroimaging domain have used virtual reality stimuli to study cortical activations associated with spatial navigation and spatial processing (Jordan et al., 2004; Jordan et al., 2001; Jordan et al., 2002; Bischof et al., 2003; Chouinard, Briere, Rainville, & Godbout, 2003; Gron et al., 2000). A subset of studies were particularly interested in uncovering the neural correlates of driving using driving games presented in the fMRI environment (Walter et al., 2001; Uchiyama, Ebe, Kozato, Okada, & Sadato, 2003; Calhoun et al., 2002; Calhoun, Pekar, & Pearlson, 2004). Some studies were only interested to explore whether a particular virtual reality equipment could be used in the context of the fMRI and EEG environment without interfering with technical and psychological constraints (Hoffman et al., 2003; Mraz et al., 2003). Although these studies have substantially increased our understanding of the cortical and subcortical mechanisms of spatial navigation and spatial processing, no study has (to my

best knowledge) directly examined the neurophysiological underpinnings of Spatial Presence using neuroscientific methods.

Therefore, the present study was designed to explore the relationship between Spatial Presence experience and cortical activations using multi-channel EEG in combination with LORETA (see Chapter 3) allowing modelling the underlying cortical structures which are supposed to generate the neurophysiological activations. In addition, psychometrical measures as well as psychophysiological measurements of heart rate and skin conductance were collected during an arousing and non-interactive virtual reality world depicting different roller coaster rides. Two independent variables were experimentally manipulated, namely the age of the user (children and adolescents) and the number of monocular spatial cues (e.g. motion parallax). Both variables have been shown to influence the Spatial Presence experience in psychometrical and behavioural Spatial Presence studies. Whereas the age of the user is negatively related with the Spatial Presence experience (e.g. Schaik et al., 2004), the number of monocular spatial cues are positively correlated with the Spatial Presence experience (Freeman et al., 1999; Ijsselsteijn et al., 1998; Ijsselsteijn et al., 2001).

7.2 Aims of the study

The aim of this study was to explore the neural correlate of high and low Spatial Presence experience in an arousing and non-interactive virtual reality world. Moreover, I addressed whether increased subjective Spatial Presence experiences in children compared to adolescents are associated with different cortical brain activation patterns.

7.3 Hypothesis

As no study has explicitly examined the cortical structures involved in Spatial Presence, I only can generate tentative hypotheses based on neuroimaging and developmental studies (see Chapter 2.5, Spatial Presence and the brain).

For both children and adolescents, I hypothesized that the subjective Spatial Presence experience is enhanced in the roller coaster conditions with many monocular spatial cues compared to the condition with only few spatial cues. Because the virtual reality world is emotional and arousing, I also expected that this enhanced Spatial Presence experience is accompanied by increased somatic and visceral reactions of the body (heart rate and skin conductance responses) as has been shown by a few psychophysiological studies in arousing virtual reality environments (e.g. Meehan, 2001; Meehan et al., 2002). Moreover, body reactions are known to activate brain regions involved in mapping and/or regulating the

somatic and visceral state of the body (e.g. insula, secondary somatosensory cortex, see for example Craig, 2002) and thus constitute an important neural correlate for conscious emotional feelings (Damasio et al., 2000). Consequently, I would expect increased activation in these brain areas in the high Spatial Presence condition along with other brain areas involved in emotion processing. Finally, I hypothesized both for children and adolescents that Spatial Presence can not occur without activation in brain areas known to be involved in spatial processing (Jordan et al., 2004; Jordan et al., 2002; Gron et al., 2000), including in particular the intraparietal sulcus and brain regions surrounding this area of the parietal cortex. This brain region generates an egocentric view by translation of the retinal coordinates to head-centre, or even body-centred, coordinates. Obviously, such an ego-centric view is essential for the experience of Spatial Presence.

Finally, I would also expect different subjective Spatial Presence experience between children and adolescents along with different brain activation patterns. An interesting structural candidate for this hypothesis is the prefrontal cortex known to be involved in the executive control system of the brain, including error detection and monitoring (Smith et al., 1999; Fuster, 2002). Based on neuroanatomical studies it is known that the frontal cortex is among the most recent brain regions to mature, implying that the tissue itself continues to develop toward adult status well into adolescence (Giedd et al., 1999; Giedd, 2004). Thus, based on the incomplete functioning of the prefrontal cortex, I suggest that the Spatial Presence experience is enhanced in young children compared to adolescents because children are less capable of cognitively controlling and monitoring the virtual experience. Accordingly, high Spatial Presence experience in an non-interactive virtual reality environment should be accompanied by reduced activation in the prefrontal cortex and in particular in the dorsal more cognitive part of this brain area (Phillips et al., 2003).

7.4 Methods and Materials

7.4.1 Subjects

12 healthy children (5 male, 7 females, between 8.4 and 10.7 years, mean age 9.2, S.D. 0.59) and 11 healthy adolescents (7 males, 4 females, between 13.9 and 17.8 years, mean age 15.8, S.D. 1.36) volunteered for the study. All subjects were recruited from various sources including family members, friends, or from local sport clubs. All subjects were consistent right-handed and native speakers of German. Handedness was confirmed using the Annett handedness questionnaire (AHQ) and the criterion for consistent right-handedness as proposed by Annett (1970). None of the subjects reported any neurological or psychiatric

disease, prior head trauma, sensory impairment or subjective cognitive impairment. All parents of the children gave informed consent and were instructed according to the ethical guidelines by the Helsinki declaration.

7.4.2 Experimental task

The subjects were sitting on a comfortable chair while they were viewing different roller coaster scenarios on a 17`` computer screen placed at a distance of 1 meter in front of them. The roller coaster scenarios were taken from commercially available roller coaster simulation software (http://www.nolimitscoaster.com/). The subjects wore headphones to hear the realistic driving noises with spatial cues included in the software. The viewing position of the roller coaster cab was arranged as if the subjects were sitting within the cab in the front seat while the cab was riding through the roller coaster scenario. During the initial control session (CONTROL) the cab drove through a horizontal roundabout track without any up or down movements and thus with only few spatial cues. During the following sessions the subjects saw roller coaster simulations during which several realistic rides were undertaken with spectacular ups and downs and thus with many spatial cues. The control scenario was used in order to control for various basic perceptual processing steps similar for all roller coaster scenarios, including form, colour, motion, and basic spatial processing. The "realistic" roller coaster drives were divided into three different sessions: (1) initial upward driving of the roller coaster cab (UP, expectation phase); (2) dynamic up- and downward driving of the cab including spectacular loops (DOWN), and (3) final horizontal drive of the cab (END). During these rides continuous electroencephalographic (EEG) and psychophysiological measures (skin conductance response: SCR, heart rate: HR) were obtained. Additionally, psychometric measures of Spatial Presence (MEC-SPQ) were obtained after the control condition and after the last realistic roller coaster ride.

7.4.3 EEG recording and analysis

EEG signals were recorded and amplified using a BrainVision 32 channel amplifier system (www.brainvision.com). Silver-silver-chloride-electrodes (Ag/AgCl) were used in association with the "Easy Cap System" (International 10-20 system, FMS Falk Minow Services, Herrsching-Breitbrunn, Germany) on which 30 electrodes were attached according to the international 10-20 system at the locations Fp1/2, F7/8, F3/4, Fz, FT7/8, FC3/4, T7/8, C3/4, Cz, TP7/8, CP3/4, CPz, P7/8, P3/4, Pz, O1/2, Oz and referenced to FCz (Reference). The electro-oculogram (EOG) was recorded from two additional electrodes placed below the outer canthus of the eyes. BrainVision Recorder and Analyzer (BrainProducts, Germany) were used

to record (electrode impedance <5 kΩ, 0.5 – 70 Hz, 500 samples/s) and analyze the data. After recording of 5 min eyes closed resting EEG, recording of EEG during the experimental sessions was performed. The total EEG recording time including prestimulation recordings was about 40 min.

All recorded EEG-epochs were carefully and individually checked for artefacts (eye blinks, horizontal and vertical eye movements, muscle artefacts, etc.) by visual inspection. Epochs that were associated even with small changes in the horizontal or vertical EOG-channel within the reference or test interval (see below) were rejected (amplitude minimum: -100 μV, maximum: 100 μV). In addition, independent component analysis (ICA) was used to extract artefact-free EEG epochs. The average number of artefact-free trials for all conditions was 80. These artefact-free epochs were recomputed to the average reference (Lehmann, 1990; Lehmann, 1988). Furthermore, a discrete Fourier transformation algorithm was applied to all extracted artefact-free epochs of data that were 2.048 s in duration each. The power spectrum from 1.5 to 30 Hz was calculated for each single epoch and then averaged across epochs. Finally, according to the hypothesis, 12 electrodes were collapsed into 3 frontal and 3 parietal electrode clusters: frontal left (F3/FC3), frontal midline (Fz/FCz), frontal right (F4/FC4), parietal left (CP3/P3), parietal midline (CPz/Pz) and parietal right (CP4/P4).

According to the surface EEG analysis in this paper, I was mainly interested in studying the changes in the Alpha-band (8-13 Hz) because changes in the power of the Alpha band have been shown to be valid indicators of cortical activation/deactivation within the frontal and parietal lobe , i.e. power in the Alpha band is negatively related to activity (Laufs et al., 2003b; Laufs et al., 2003a; Gamma et al., 2004). The percentage change in Alpha band power between the control condition (CONTROL roundabout riding) and the three sessions of realistic roller coaster riding (UP, DOWN, and END) were calculated using the following formula: ERD/ERS = ((band power reference – band power test) / (band power reference)) × 100 (Pfurtscheller, 1989). Note that positive values indicate a relative power decrease in the Alpha band (ERD) and negative values indicate a relative power increase (ERS). Thus, ERD indicates cortical activation while ERS indicates cortical deactivation (note that this is only true for the Alpha-band, see Chapter 3.2.4.1). These ERD/ERS at the 6 electrode clusters were thereafter used for further statistical analyses.

7.4.4 Psychophysiological and psychometrical measurements

According to Meehan (2001) physiological Presence means that a user is "responding physiological to the mediated environment in a manner consistent with human response to similar real situations". Therefore, in addition to EEG, measurements of heart rate (HR), and

skin conductance responses (SCR) were made during the experiment by using a commercially available device (PAR-PORT manufactured by Hogrefe Company, Germany). For SCR recording, electrodes were attached to the thenar and hypothenar areas on the palm of the left hand. Quantification of SCR's entailed measurement and summation of the SCR amplitude and division by the length of the conditions in seconds due to different durations of the 4 conditions. In addition, log-transformation (log[SCR+1]) was used to normalize the SCR amplitude data. Furthermore, the self-location subscale of the MEC-SPQ questionnaire was used to obtain psychometric measures of Spatial Presence (MEC-Spacial Presence Questionnaire; Vorderer et al., 2004). This questionnaire (8 items, 5-point scales ranking from "1 = I do not agree at all" to "5 = I agree fully") was administered after the control condition and immediately after the last of the five roller coaster rides. The scale measures the subjective impression how much the subjects felt to be in the middle of the action of the roller coaster ride rather than merely observing it.

7.4.5 Statistical analysis

The ERD/ERS values were analyzed with a four-way ANOVA with the following repeated measurements factors: “roller coaster ride” (UP, DOWN, END), “region” (frontal vs. parietal), and “hemisphere” (left, midline, and right). In addition, a between-subjects factor was used to compare children with adolescents. Furthermore, two three-way ANOVA's with repeated measurements on each factor (“roller coaster ride”: UP, DOWN, END; “region”: frontal, parietal; “hemisphere”: left, midline, right) were conducted separately for children and adolescents. For each psychophysiological measurement (HR, SCR), two-way ANOVAs were performed with the factors “roller coaster ride” (Control, UP, DOWN, END) as repeated-measurement factor and “group” (Children vs. Adolescents) as a grouping factor. To analyse the self-location scale of the MEC-SPQ, which was answered by the subjects after the control condition and after the 5 roller coaster rides, a repeated-measures ANOVA was conducted with the factors “roller coaster ride” (Control, Roller Coaster Ride) and “group” (GROUP 2: Children, Adolescents). For all repeated measurement ANOVAs the multivariate approach for factors comprising more than 2 conditions was used to avoid anticonservative estimation of F-values due to possible violations of homoscedasticity (O'Brien & Kaiser, 1985). Because it is more important to demonstrate the empirical effect of a treatment rather than to calculate p values, I also report effect size measures independent from sample size (Cohen, 1969). As effect size measure ETA^2 was calculated, which is the estimated variance due to the treatment in relation to the total variance. Thus, ETA^2 describes the variance which is due to the experimental effect. All statistical analyses were performed using the statistical software

package SPSS PC (version 11.5). Results were considered significant at the level of $p<0.05$. In case of a significant multivariate effect post hoc paired t-tests were computed using the Bonferroni correction according to Holm (1979).

7.4.6 LORETA

For the purpose of displaying intracerebral EEG-data, in addition to the ERD/ERS two-dimensional scalp map analysis, the LORETA inverse solution method was employed (Pascual-Marqui et al., 1999; Pascual-Marqui et al., 1994) which computes, from the recorded scalp electric potential differences, the three dimensional distribution of the electrically active neuronal generators in the brain as a current density value (A/m^2) at each voxel. LORETA solves the inverse problem based on the assumption that the smoothest of all possible activity distributions is the most plausible one. This assumptions is supported by electrophysiology, where neighbouring neuronal populations show highly correlated activity (e.g. Haalman & Vaadia, 1997). The version of LORETA employed here used a three-shell spherical head model registered to the digitized Talairach and Tournoux (1988) atlas (Brain Imaging Centre, Montreal Neurological Institute). The registration between spherical and the Talairach and Tournoux head geometry used the realistic EEG electrode coordinates reported by Towle et al. (1993). Further, the source solution space was limited to cortical gray matter and hippocampi according to digitized probability atlas provided by the Montreal Neurologic Institute (number of voxels: 2394; voxel dimension: $7mm^3$). Voxels were defined as gray matter if their probability of being gray matter was greater than (a) 33%, (b) exceeded the probability of being white matter, and (c) exceeded the probability of being cerebrospinal fluid. It has been shown in numerous experiments that the method is capable of correct localization of primary sensory cortices, epileptic foci, language processing, face processing and emotion processing areas with fairly low errors (Esslen et al., 2004; for a recent review see Pascual-Marqui et al., 2002).

Whole brain analysis using voxelwise paired t-tests examined differences between the CONTROL and DOWN conditions separately for children and adolescents in six frequency bands according to Kubicki et al.(1979): Delta (1-3 Hz), Theta (4-7 Hz), Alpha (8-12 Hz), Beta1 (13-18 Hz), Beta2 (19-21 Hz), Beta 3 (22-30 Hz). Based on current knowledge about the functional significance of these EEG bands, I take the Beta bands as indicating neural activation while increasing power in the Alpha and Theta band generally indicate decreased neural activation (Oakes et al., 2004). Due to the extremely conservative non-parametric randomization statistic used by the LORETA-Key software (corrected for multiple tests) I will accept condition differences as significant if the p value is <0.10.

7.5 Results

7.5.1 Self-Location rating (MEC-SPQ)

The highly significant main effect of "roller coaster ride" ($F_{(1,21)}$ = 35.34, p<0.001, ETA^2 = 0.627) was due to the higher rating of self-location during the roller coaster rides compared to the control condition for both children and adolescents. Furthermore, a group effect was observed ($F_{(1,21)}$ = 4.30, p=0.05, ETA^2 = 0.170), indicating that the children experienced stronger Spatial Presence than the adolescents.

7.5.2 Skin conductance responses and heart rate

As Figure 11.10 (page 148) illustrates, there was a highly significant main effect of "roller coaster ride" ($F_{(3,19)}$ = 17.55, p < 0.001, ETA^2 = 0.735), indicating the largest SCR sum amplitude for UP, intermediate for DOWN and lowest for END and Control. In addition, SCR amplitude and the subjective Spatial Presence experience as measured with the MEC-SPQ subscale showed one significant correlation and one trend for a significant positive correlation (SCR UP/Self-Location: r = 0.409, p=0.053; SCR DOWN/Self-Location: r = 0.485, p<0.05), demonstrating that subjects who rated high on the MEC-SPQ subscale also showed increased SCR's in the most arousing conditions of the experiment (UP and DOWN). Surprisingly, no significant differences regarding HR measures were observed.

7.5.3 ERD/ERS of Alpha Power (Children and Adolescents)

The four-way ANOVA for the dependent variable ERD/ERS revealed a significant four-way interaction between all independent variables ("roller coaster ride" * "group" * "region" * "hemisphere": $F_{(4,18)}$ = 4.2, p = 0.014, ETA^2 = 0.485); thus, all other main effects or interactions should be interpreted with reluctance. However, "region" and "region" * "roller coaster ride" showed a strong effect on the ERD/ERS values ("roller coaster ride": $F_{(1,21)}$ = 14.4, p < 0.001, ETA^2 = 0.407 and "roller coaster ride" * "region": $F_{(2,20)}$ = 11.5, p < 0.001, ETA^2 = 0.536), indicating increased ERD (cortical activity) at parietal electrode clusters compared to the frontal electrode clusters and this effect was most pronounced in the DOWN (dynamic roller coaster ride) condition. In addition, the main effect of "hemisphere" ($F_{(2,20)}$ = 4.7, p = 0.021, ETA^2 = 0.320) and the interaction effect of "region" * "hemisphere" ($F_{(2,20)}$ = 5.8, p = 0.01, ETA^2 = 0.366) demonstrated topographically the largest positive percentage change (ERD) at the midline parietal electrode cluster. Most interestingly, a significant interaction between "region" * "group" was observed ($F_{(1,21)}$ = 4.3, p = 0.05, ETA^2 = 0.171), which was qualified by increased frontal ERD for adolescents compared to children. In other words, children showed reduced activity at frontal electrodes (see Figure 11.11 on page 148).

Since the four-way interaction was significant and four-way interactions are difficult to interpret, two additional three-way ANOVA's were calculated separately for children and adolescents.

7.5.4 ERD/ERS of Alpha Power (Children)

The three-way ANOVA revealed two main effects for "roller coaster ride" ($F_{(2,10)} = 4.1$, $p = 0.05$, $ETA^2 = 0.451$) and "region" ($F_{(1,11)} = 11.9$, $p < 0.01$, $ETA^2 = 0.519$) and a significant interaction effect for "region" * "roller coaster ride" ($F_{(2,10)} = 7.8$, $p < 0.01$, $ETA^2 = 0.611$). Figure 11.12 (page 149) depicts this significant interaction which clearly demonstrates the dissociation between frontal and parietal electrodes during the roller coaster ride in children. They showed the strongest activations at parietal leads during the DOWN condition and significantly reduced cortical activity both in the UP and END conditions. By contrast, frontal electrodes demonstrated a different pattern which was qualified by an increase in cortical activation in the UP condition and a significant cortical decrease of activation in the DOWN and END conditions. In addition, both in the DOWN and END conditions, the frontal activation patterns compared to the parietal patterns differed significantly.

7.5.5 ERD/ERS of Alpha Power (Adolescents)

The three-way ANOVA showed a significant interaction effect of "region" * "roller coaster ride" ($F_{(2,9)} = 4.5$, $p = 0.043$, $ETA^2 = 0.503$; see Figure 11.13 on page 149), indicating, similar to children, the highest ERD in the DOWN and UP condition and significantly reduced ERD in the END condition at parietal electrode clusters. In contrast to the activation pattern of the children, adolescents showed increased cortical activation at frontal electrodes in all three conditions (UP, DOWN, END). Additionally, frontal and parietal ERD's differentiated in the DOWN condition. Table 10.5 (page 138) summarises the means (± SE) of the ERD and ERS values for both groups broken down for all conditions.

7.5.6 LORETA

As expected, the statistical comparison between the CONTROL and DOWN condition (separately for children and adolescents) using voxel-wise paired t-tests for all frequency-bands revealed significant differences in the Alpha-band (8-12 Hz) for both groups. Furthermore, two bands, the Theta band (4-7 Hz) in children and the Beta2 band (19-21 Hz) in adolescents, showed trends towards significance on the 10% level. No other significant results or trends towards significance in the other frequency bands were observed (all $p > 0.25$). Table 10.6 (page 139) summarizes all findings separately for children and adolescents. Alpha band activity was decreased both in children and adolescents in the DOWN condition

mainly in parietal and occipital brain regions, indicating increased activity in the DOWN condition in regions known to be essentially involved in processing of visual spatial information. In children, this activity increase was most prominent on the right hemisphere while in adolescents a more bilateral activation pattern was found (Figures 11.14 on page 150 and 11.18 on page 154). A further decrease in the Alpha band activity in both groups in the DOWN condition was observed in the posterior cingulate gyrus. Interestingly, children but not adolescents demonstrated increased Alpha band activity (indicating decreased neural activity) in the DOWN condition in frontal regions (right inferior frontal gyrus and right middle frontal gyrus) known to be involved in various executive functions. In addition, in children the Alpha band activity was increased during the DOWN condition bilaterally in the insula and the left postcentral gyrus (Figure 11.16 on page 152). Noteworthy, no Alpha band increase in the DOWN condition could be observed in adolescents. In contrast, adolescents revealed a marked increase of Beta2 activity in left precentral gyrus, left inferior frontal gyrus and left insula during the DOWN condition (Figure 11.19 on page 155). Finally, in the DOWN condition children showed decreased Theta activity in right inferior parietal lobe and right precuneus (Figure 11.15 on page 151) and increased Theta activity in bilateral superior frontal gyrus and left middle temporal gyrus, respectively (Figure 11.17 on page 153).

7.6 Discussion

The major aim of the present study was to explore whether different Spatial Presence experiences are associated with typical cortical activation patterns. For this, different VR roller coaster scenarios were used in the context of EEG measurements. One scenario was a simple horizontal roundabout tour (low Spatial Presence condition), while the other scenarios were more realistic roller coaster rides including the typical ups, downs and loops (high Spatial Presence condition). For the more realistic roller coaster scenario I also analysed different sessions of the ride (UP, DOWN, and END) because I hypothesized that each session would have different impact on the perceptual and emotional system.

As hypothesized, I found that compared to the control condition experiencing a virtual roller coaster ride evoked in both groups (children and adolescents) (1) strong Spatial Presence experiences, (2) increased skin conductance responses and (3) with respect to the surface EEG (for which the Alpha band was analyzed) strong event-related power decreases over parietal leads (ERD), indicating cortical activation in this region. Moreover, children and adolescents showed a different activation pattern at frontal electrode sides. Whereas children revealed event-related power increases (ERS) during the DOWN and END conditions (indicating

decreased activation), adolescents consistently showed event related power decreases (ERD) in the UP, DOWN and END condition (indicating increased cortical activation over frontal electrodes). Interestingly, this differential cortical activation pattern was also associated with stronger Spatial Presence experiences in children compared to adolescents. Using LORETA (low resolution electrical tomography) to calculate the intracerebral electrical sources for the surface EEG I found that the above mentioned EEG activity pattern on the scalp was generated by a distinct network of brain areas known to be involved in visual spatial processing (inferior and superior parietal gyrus, precuneus), the control of executive functions (inferior, middle and superior frontal gyrus), the mapping and regulating of body sensations (insula, postcentral gyrus) and emotion processing (posterior cingulate, cingulate gyrus). The LORETA results mainly confirmed the ERD findings at frontal and parietal electrode positions, however, with increased spatial resolution. Thus, LORETA also revealed that children showed reduced cortical activity, whereas adolescents showed increased cortical activity at frontal brain areas, suggesting that children and adolescents use different neural assemblies to process the visual cues and the Spatial Presence experience associated with the roller coaster ride.

In the following, the findings will be discussed in more detail separately for each brain region.

7.6.1 Activation in the parietal lobe

As hypothesized, both groups demonstrated the largest ERD values (indicating cortical activation) at parietal electrode positions in the DOWN condition as well as decreased intracerebral electric activity (in the Alpha or Theta band) during the DOWN compared to the CONTROL condition in the posterior cingulate, superior parietal lobe (bilaterally in adolescents), the inferior parietal lobe (right-side in children), and the precuneus (right sided in children). These areas are known to be involved in various steps of spatial processing as well as mental rotation tasks and constitute a neural correlate for the ego-centric view (Jordan et al., 2004; Jordan et al., 2002; Jordan et al., 2001; Gron et al., 2000). As discussed in Chapter 2.5, this ego-centric view is in my opinion a necessary prerequisite for the experience of Spatial Presence. Moreover, the finding of increased activation in these brain areas in the high compared to the low Spatial Presence condition is consistent with the “intensity check” mechanism proposed in the neuropsychological model by Jancke (2005), indicating that the strength of activation in these areas is important in determining the Spatial Presence experience.

7.6.2 Activation in the insula

A potential core region for generating Spatial Presence experiences in an arousing virtual reality world might be the insula for which neural activation changes during the DOWN compared to the CONTROL condition were found in both groups. The insula receives homeostatic afferents from several modalities, including temperature, pain, proprioception, and the viscera and, thus, is involved in the mapping of body related sensations (for a review see Craig, 2002). In addition, insular activation was also found in several brain imaging studies during aversive emotional stimulation that also evoke visceral/somatic sensations (Phan et al., 2002). Thus, the insula seems to constitute a primary interoceptive image of homeostatic afferents. Interestingly, in children I observed increased neural electric activity bilaterally situated in the insula and the ventral part of the postcentral gyrus (which is also involved in the mapping of body sensations) in the Alpha band, while the adolescents showed increased neural activity in the insula in the Beta2 band. Whereas activity in the Beta2 band can be taken as activation (e.g. Oakes et al., 2004), the Alpha band is (in most paradigms and brain regions) negatively correlated with neural activity as mentioned above (Laufs et al., 2003a). However, the insula seems to be an exception, i.e. Alpha power in the insula is positively correlated with neural activity (Goldman, Stern, Engel, Jr., & Cohen, 2002; Sadato et al., 1998). Thus, I conclude that increased insula activity for the Alpha band indicates increased insular activation during the realistic roller coaster ride in children. The reason why adolescents and children differ with respect to the different activation of the Alpha and Beta2 bands is difficult to explain. Perhaps there is a general age-dependent effect on the neural activation pattern in the insula. However, I hypothesize that insula and postcentral gyrus activation reflect increased somatic and visceral reactions during the roller coaster ride compared to the Control condition. The importance of somatic and visceral sensations for the experience of Spatial Presence (in an arousing virtual reality) is further confirmed by the observed positive correlations between skin conductance responses in the UP and DOWN conditions and the psychometrical measures of Spatial Presence. Such positive correlations were also found in classical psychophysiological studies of Spatial Presence (e.g. Meehan et al., 2002; Wiederhold et al., 2002b).

7.6.3 Activation in the posterior cingulate cortex

In addition, another brain structure, the cingulate gyrus, is strongly activated in children and adolescents in the DOWN condition (indexed by reduced neural electric activity in the Alpha band). This brain region is involved in various functions including emotional stimulus

processing (e.g. Damasio et al., 2000; Maddock et al., 1997; Esslen et al., 2004), episodic memory function (Maddock et al., 2003), and spatial attention (Mesulam et al., 2001) and is strongly connected with frontal and temporal cortical areas (Morris et al., 1999; Allison et al., 2000). Thus, I hypothesize that the processing centres in the parietal cortex which were strongly activated in this study as demonstrated above, stimulated the emotional centres via various routes including the posterior cingulate. These emotional centres (limbic system) might have generated various emotional reactions including fear, joy or interest leading to an increased Spatial Presence experience in the roller coaster condition.

7.6.4 Activation in the temporal pole

Children but not adolescents showed an increased intracerebral electric activity in the left middle temporal gyrus extending into the temporal pole for the Theta band. This region plays a key role in various functions, including autobiographical and episodic memory (Maguire & Mummery, 1999), face recognition (Sergent, Ohta, & MacDonald, 1992), and linguistic as well as emotional language processing (Braak, Braak, Yilmazer, & Bohl, 1996; Tzourio, Crivello, Mellet, Nkanga-Ngila, & Mazoyer, 1998; Dupont, 2002, for a recent review). In addition, Theta oscillations in the temporal lobe have been implicated in spatial navigation in animals and in particular have been linked to the encoding and retrieval of spatial information in the hippocampus in rodents (Skaggs et al., 1996; O'Keefe et al., 1993). Human navigation studies have recently confirmed these findings in showing increased Theta activity over temporal leads (Bischof et al., 2003; Kahana et al., 1999). Related to the present study, these findings might indicate that children encode spatial information during the roller coaster rides. However, I can not give a plausible explanation why adolescents do not show this activation pattern in the temporal cortex during the roller coaster ride.

7.6.5 Functional dissociation in the frontal cortex between children and adolescents

Most interesting as hypothesized, children and adolescents showed a clear dissociation with respect to the activation of frontal brain areas, revealed both by the surface EEG analysis (ERD/ERS) as well as by the intracortical electrical analysis (LORETA). Regarding the ERD results, both groups showed in the UP condition (anticipation phase) increased cortical activation at frontal electrodes sides along with the highest skin conductance reactions, indicating highest arousal in the anticipation phase of the high Spatial Presence condition. In contrast, children demonstrated both in the DOWN and END condition significantly reduced cortical activation at frontal electrode sides, while adolescents showed a similar frontal activation pattern in the UP, DOWN and END conditions, demonstrating no activation

decrease at frontal electrode positions. LORETA confirmed this different frontal activation pattern in children and adolescents in the DOWN compared to the CONTROL condition. Adolescents revealed increased electric activity in the left inferior frontal gyrus and the left precentral gyrus in the Beta2 band. Children on the other hand showed increased electric activity in the right inferior and middle frontal gyrus in the Alpha band as well as increased electric activity in the Theta band bilaterally in the superior frontal gyrus. Based on current knowledge about EEG measurements increased electric activity in the frontal lobe in the Alpha and Theta bands indicate neural deactivation, while increased electric activity in the Beta2 band indicates increased neural activation (Oakes et al., 2004; Laufs et al., 2003a). Accordingly, adolescents showed increased neural activation while children on the other hand showed decreased activation in the described frontal structures. Interestingly, these frontal structures are known to be involved in the regulation of various executive functions.

For example, the inferior frontal gyrus is involved in specific functions including modulation social behaviour (Decety & Chaminade, 2003), controlling complex sequential actions (Corballis, 1991; Corballis, 1992), simulating or anticipating of actions (Adam et al., 2003), response inhibition (Konishi et al., 1999; Rubia, Smith, Brammer, & Taylor, 2003; Taylor et al., 2003; Taylor, Kornblum, Lauber, Minoshima, & Koeppe, 1997; Menon, Adleman, White, Glover, & Reiss, 2001), attentional processes (Jancke & Shah, 2002; Noesselt, Shah, & Jancke, 2003; Heyder, Suchan, & Daum, 2004; Corbetta et al., 2002), set shifting (Winconsin Card sorting test, Konishi et al., 1999; Nakahara, Hayashi, Konishi, & Miyashita, 2002) or detection of incongruities (Moran et al., 2004). However, and more important for the present study are theoretical assumptions pinpointing the right frontal cortex as a major part of a frontoparietal attention network including the inferior and middle frontal gyrus as well as the temporo-parietal junction. This network has been shown to operate as a target detection and alarm system directing attention to novel salient events in situations when the system is strongly engaged in processing other stimuli, in this case the virtual reality environment (for a review see, Corbetta et al., 2002). Damage to these structures abolish the P300 which is known to be triggered by the detection of infrequent or novel stimuli embedded in a temporal stream of standard stimuli (Daffner et al., 2000b; Knight & Scabini, 1998). In addition, it has been shown that lesions of the right frontal cortex specifically impair vigilance (Wilkins, Shallice, & McCarthy, 1987; Daffner et al., 2000a). Finally, the dorsal parts of the frontal gyrus (superior frontal gyrus) are known to be involved in associating sensory stimuli with motor responses (Jancke, Loose, Lutz, Specht, & Shah, 2000; Lutz, Specht, Shah, & Jancke, 2000; Toni, Schluter, Josephs, Friston, & Passingham, 1999). The prominent role of these

areas in processing sensorimotor associations has also been shown by human lesion studies. Patients with lesions in these areas show a kind of “stimulus driven” behaviour which is characterized by inevitably grasping and manually exploring nearly each external stimulus they encounter (Heilman et al., 2003).

Whether the aforementioned psychological processes are indeed active during the roller coaster ride is difficult to decide. However, I believe that the results of the aforementioned neuroimaging and lesion studies support the idea that adolescents more strongly controlled and monitored the ongoing activities inside and outside the focus of attention and, thus, these mental operations diminished their Spatial Presence experience. In contrast, decreased activation of these frontal structures in the context of strong activations in parietal areas in younger children might indicate that children were strongly driven by the salient stimuli of the virtual reality environment and neither controlled (or at least to a significant lesser degree) the Spatial Presence experience nor monitored the surrounding environment. As a consequence, their Spatial Presence experience was markedly enhanced.

I hypothesize that this reduced frontal activation in children and consequently reduced executive functions might depend on the non-matured frontal cortex. As mentioned in the introduction, the frontal lobe (especially the white matter) matures until the age of young adults (Giedd, 2004; Giedd et al., 1999). Thus, the younger children of this study group were examined during a cortical maturation phase during which the frontal cortex is not fully developed and consequently, the executive functions controlled by this lobe are also not fully functional. Further evidence for this functional "impairment" of the frontal lobe in children comes from behaviour and neuroimaging developmental studies. For an example, the ability to inhibit prepotent responses markedly increases from childhood into early adulthood and reaction time improvements for both response execution and response inhibition are observed between the ages of 6 and 20 (Band, van der Molen, Overtoom, & Verbaten, 2000; Williams, Ponesse, Schachar, Logan, & Tannock, 1999). Interestingly, neuroimaging studies have shown in response inhibition tasks (Go/NoGo) a positive correlation between activation and age in the left inferior frontal gyrus which was strongly activated in adolescents but not in children in the present roller coaster study. In contrast, children showed in these studies a more extensive activation in discrete regions of the prefrontal cortex indicating an increased demand and inefficient recruitment of brain regions subserving executive functions (Rubia et al., 2000; Tamm, Menon, & Reiss, 2002).

Taken together, younger children are obviously more prone to experience Spatial Presence during a virtual roller coaster drive due to a not fully developed prefrontal lobe leading to

reduced control and monitoring of the experimental situation. This anatomical "impairment" might also be the reason for the well known facts that young children experience strong emotions when watching comic movies, reading books and playing computer games. Extremely positive or negative emotions can easily be evoked in young children using stimuli which would never evoke strong emotions in adolescents or adults (Luna et al., 2001; Ridderinkhof et al., 1995; Bjorklund et al., 1990).

7.6.6 Limitations

Not surprisingly, despite of the promising results, many questions concerning the neurophysiological underpinnings of Spatial Presence are still unanswered and suggest future studies to further elucidate the functional significance of these findings, especially the functional significance of the dissociation between frontal and parietal cortical structures which seems to play a pivotal role in this study in modulating Spatial Presence experience. Will the content of any particular environment evoke similar frontal and parietal brain activation? Or can we only observe this frontal activation pattern in passive viewing Spatial Presence conditions and not in virtual reality worlds where the subjects can interact with the surrounding environment? In other words, if the content of the virtual environment is an everyday situation and not an arousing roller coaster ride, what brain activation pattern can be found? There is no doubt that the brain activation pattern will change significantly if one can freely move around (leading to activation in the motor and premotor cortex) or has to solve cognitive problems (leading at least to activation in the short and long-term memory system and additional parts of frontal cortex) in a virtual reality world. Nevertheless, it might still be the case that subjects who show a decreased activity in some mid-dorsal brain regions and especially some areas of the inferior frontal gyrus will report an increased Spatial Presence experience.

Surprisingly, heart rate showed no reaction differences in the high compared to the low Spatial Presence condition. In contrast, a recent study (Bördlein & Kuschyk, 2004) on a real roller coaster demonstrated strong heart rate increases in the UP and DOWN condition (compared to a resting baseline). These findings indicate that there is, not surprisingly, still a gap between the virtual reality simulation and reality. Nevertheless, the virtual reality seems to be a good simulation because skin conductance responses (a very sensitive arousal measure) in the virtual reality environment and heart rate responses on the real roller coaster showed a similar reaction pattern, which was qualified by the highest psychophysiological body reactions in the UP condition, intermediate body reactions in the DOWN condition and lowest

body reactions in the END condition. These findings indicate a good external validity of the virtual reality simulation used in this study.

7.7 Conclusion

Summing up, the salient spatial cues delivered by the roller coaster scenarios evoked strong and overwhelming activations within the parietal processing centres which in turn stimulated the insula as core region for generation body sensations and the posterior cingulate which is strongly involved in emotion processing. Beside this activation route, there also exists a frontal activation route obviously exerting control over the first stimulus driven route. These frontal areas are involved in controlling the overwhelming and salient spatial and body cues evoked by the roller coaster scenario and are monitoring the ongoing activities outside the focus of processing. Therefore, the results of this study imply that strong Spatial Presence experiences in an arousing and non-interactive virtual reality world are associated with markedly increased activity in parietal/occipital areas of the brain together with decreased activity in frontal structures involved in the executive system of the brain. In addition, autonomic somatic reactions (SCR) are increased along with activation in brain structures known to be involved in the somatic and visceral representation of the body state and emotion processing.

8 General Discussion

This dissertation consists of three experimental studies seeking to elucidate the neural correlates of strong emotional experiences as well as the neural correlates of Spatial Presence. In this section, the key findings will be briefly summarized, followed by a general integrative discussion of the findings of all three studies focusing similarities regarding processes of strong emotional experiences as well as processes of controlling and modulating these strong feeling states. Finally, a short conclusion and outlook for future studies will be given.

8.1 Summary of the results

8.1.1 Study A and B: The emotional power of music

Two studies addressed the question whether the combined presentation of congruent emotional visual and musical stimuli enhance the emotional brain processing compared to the single presentation from one modality. Surprisingly, this enhancement effect is completely understudied in brain research to date. Most of the emotional brain studies used visual stimuli to evoke emotions (e.g. Lee et al., 2004; Hariri et al., 2002; Esslen et al., 2004) and only a few have tried to evoke emotions using musical excerpts (e.g. Blood et al., 2001; Brown et al., 2004; Altenmuller et al., 2002). Nevertheless, the results of these few musical studies are impressive, showing activation in brain areas known to be involved in reward/motivation, emotion and arousal, including for example ventral striatum, thalamus, midbrain, orbitofrontal cortex and insula.

Therefore, an EEG and fMRI study was designed to explore the neural underpinnings of the proposed emotional enhancement effect. Highly arousing pictures of the International Affective Picture System (Lang et al., 1995) and classical musical excerpts (Krumhansl, 1997) were chosen to evoke the three basic emotions of happiness, sadness and fear. The emotional stimuli modalities were presented either alone (only emotional pictures were presented alone in the fMRI study) or congruent combined. In addition to the measurements of brain activity, psychometrical measures (valence and arousal rating scales) were collected in both studies. Furthermore, psychophysiological body reactions (skin conductance responses, heart rate, respiration, temperature) were obtained in the EEG study to objectively discriminate processes of cognitively evaluating emotions on the one hand and strongly feeling and experiencing emotions on the other hand.

Results of the two studies strongly confirmed the proposed enhancement effect. The combined condition compared to the single presentation of emotional pictures was qualified

by (1) increased involvement and valence ratings, (2) increased psychophysiological arousal measures (skin conductance responses, heart rate, respiration) as well as (3) enhanced general brain activation measured at anterior and posterior electrode clusters on the scalp (EEG study). Due to the increased spatial resolution, the fMRI study could reveal more distinct cortical as well as subcortical brain activation patterns, indicating that strong emotional experiences in the combined condition were associated with activation in brain structures proposed to compose the ventral system of emotion processing (Phillips et al., 2003), including amygdala, ventral frontal cortex, striatum, insula, and brainstem nuclei as well as hippocampus and parahippocampus (proposed by the author of this dissertation to be also part of the ventral system of emotion processing). Moreover, increased activation was found in the combined compared to the picture condition in extrastriate visual processing areas (fusiform gyrus), in brain areas known to be involved in neutral and emotional visual-auditory integration processes (Mesulam, 1998; Adolphs et al., 2002) as well as in the auditory cortex (Zatorre, Belin, & Penhune, 2002). In contrast, the picture condition only showed an activation increase in the cognitive more dorsal system for emotion processing (Phillips et al., 2003), mainly in the right dorsolateral prefrontal cortex. These findings regarding the brain activation pattern along with the psychometrical as well as psychophysiological arousal measures point to a clear dissociation between the picture and the combined condition, indicating that emotional pictures alone activate a more cognitive emotional perception process, whereas combined presentations of emotional visual and musical stimuli evoke rather automatically strong emotional experiences and feelings.

The musical condition alone, only measured in the EEG study, demonstrated a clear dissociation between the psychometrical and psychophysiological involvement measures and the cortical brain activation pattern. Whereas the musical excerpts evoked strong emotional reactions, the cortical activation substantially decreased compared to both the combined and picture condition, indicating that musical stimuli alone activate an more internal mode of brain function which is characterized by cognitive and emotional processes revolving around the subject's internal state instead of current external events and circumstances (Gusnard et al., 2001; Raichle et al., 2001). Accordingly, fronto-parietal attention networks (Corbetta et al., 2002) preparing the subject to react adequately to external events and circumstances show diminished activations, while probably subcortical structures, which can not be detected using EEG, show enhanced activations leading to intense emotional feelings and experiences (Blood et al., 2001; Damasio et al., 2000).

Taken together, both studies suggest that strong emotional experiences which direct attention to external events and circumstances can not be evoked using either picture or musical stimuli alone. Only the combined presentation of visual and musical emotional stimuli can evoke strong emotional experiences and feelings focusing external events and circumstances.

8.1.2 Study C: A neural correlate of Spatial Presence

The goal of the third study of this dissertation was to elucidate the neural underpinnings of Spatial Presence. Surprisingly, no brain imaging study has ever explored the neural correlate of Spatial Presence which occurs in virtual reality and is considered "a sense of being there" which "occurs when part or all of a person's perception fails to accurately acknowledge the role of technology that makes it appear that s/he is in a physical location and environment different from her/his actual location and environment in the physical world"(Schubert et al., 2001).

Therefore, the present study was designed to explore the relationship between Spatial Presence experience and cortical activations using multi-channel EEG in combination with LORETA (see Chapter 3) allowing modelling the underlying cortical structures which are supposed to generate the neurophysiological activations. In addition, psychometrical measures as well as psychophysiological measurements of heart rate and skin conductance were collected during an arousing and non-interactive virtual reality world depicting different roller coaster rides. Two independent variables were experimentally manipulated, namely the age of the user (children and adolescents) and the number of monocular spatial cues (e.g. motion parallax). Both variables have been shown to influence the Spatial Presence experience in psychometrical and behavioural Spatial Presence studies. Whereas the age of the user is negatively related with the Spatial Presence experience (e.g. Schaik et al., 2004), the number of monocular spatial cues are positively correlated with the Spatial Presence experience (Freeman et al., 1999; Ijsselsteijn et al., 1998; Ijsselsteijn et al., 2001).

12 healthy children and 11 healthy adolescents were watching different virtual roller coaster scenarios. During a control session with few spatial cues, the roller coaster cab drove through a horizontal roundabout track. The following realistic roller coaster rides consisted of spectacular ups, downs and loops and thus consisted of many spatial cues. As expected, it was found that compared to the control condition experiencing a virtual roller coaster ride evoked in both group strong Spatial Presence experiences, increased skin conductance reactions and activations in parietal brain areas known to be involved in spatial navigation (Jordan et al., 2004; Jordan et al., 2002; Gron et al., 2000). In addition, brain areas were strongly activated which receive homeostatic afferents from somatic and visceral sensations of the body

(Damasio et al., 2000; Craig, 2002). Most interesting, children compared to adolescents reported higher Spatial Presence experiences and demonstrated a different frontal activation pattern. While adolescents showed increased activation in prefrontal areas known to be involved in the control of executive functions (Fuster, 2002), children demonstrated decreased activity in these brain regions. Interestingly, recent neuroanatomical and neurophysiological studies have shown that the frontal brain continues to develop to adult status well into adolescents (Giedd et al., 1999; Giedd, 2004). Thus, the result of this study implies that the increased Spatial Presence experience in children may result from the not fully developed prefrontal cortex and an inadequate or weak control function of the prefrontal cortex.

Taken together, these findings indicate that the Spatial Presence experience in an arousing and non-interactive virtual reality world is associated with (1) strong activation in parietal and occipital areas of the brain together with (2) decreased activation in prefrontal structures involved in the executive control system of the brain. In addition, (3) autonomic body reactions are increased along with activation in brain structures known to be involved in the somatic and visceral representation of the body state and emotion processing.

8.2 A neural correlate of strong emotional experiences

One of the main goals of this dissertation was to elucidate a neural correlate of strong emotional experiences. The network involved in these strong experiences should be the same no matter what kind of paradigm is used to evoke strong, overwhelming emotions. For this purpose, two completely different paradigms were compared, namely an arousing virtual reality world depicting roller coaster rides as well as emotions evoked by visual and musical stimuli. Interestingly, one cortical structure was strongly activated in both paradigms – the insula. The insula is known to be involved in the mapping and regulating of somatic and visceral body states and is thought to constitute a neural basis for conscious feelings (Damasio et al., 2000; Craig, 2002). Therefore, the study of this dissertation is in line with the literature, indicating that somatic and visceral reactions of the body and the mapping of these body states in the insula are an essential part of strong conscious feelings and experiences.

However, only one brain imaging method of this dissertation had the possibility to localize activations in subcortical structures and therefore only cortical structures could be compared between the two paradigms. This is a major limitation because the musical condition in the EEG study (study A, Chapter 5) has demonstrated that strong emotional feelings can arise despite of decreased cortical activations. Obviously, subcortical structures play also a pivotal role in the process of emotions and in particular in strong emotional experiences. For example,

in the fMRI study of this dissertation (Study B, Chapter 6) a strong positive correlation was found between activations in the amygdala and the subjective arousal ratings, indicating that this subcortical structure contributes importantly to a state of strong and conscious emotional feelings. Moreover, besides the activation in the insula and the ventral prefrontal cortex, the network involved in strong emotional experiences was composed of subcortical structures, including the amygdala, hippocampus, parahippocampus, striatum and brainstem nuclei. These structures belong to a network (ventral system) proposed to be important for the identification of the emotional significance of the stimuli, the production of the affective states (including autonomic, neuroendocrine, and somatomotor responses, as well as conscious emotional feeling), and automatic and autonomic regulation of emotional responses (Phillips et al., 2003, see Chapter 1.1.3). Therefore, the fMRI study of this dissertation could strongly confirm that emotional experiences mainly evoke activations in this proposed ventral system for emotion processing. However, future studies are needed to clearly elucidate which cortical and subcortical structures are important for the conscious state of emotional feelings. The studies of this dissertation suggest that both cortical and subcortical structures are involved in this process of strong and conscious emotional feelings, including the insula as an important cortical structure as well as the amygdala as an essential subcortical structure.

8.3 A neural correlate of cognitive control processes

For survival and adequate social functioning, a system for controlling and cognitively evaluating strong emotional reactions is also essentially important. Again, I propose that such a system should be similar active no matter what kind of paradigm is used. Interestingly, both paradigms used in this dissertation revealed a similar network in the prefrontal brain, mainly in the lateral and dorsal part, showing enhanced activity whenever the emotional experiences and the Spatial Presence experiences were diminished, respectively. No subcortical or other cortical structures were involved in this control process. These findings are again in line with the proposed dorsal system for emotion processing (Phillips et al., 2003, see Chapter 1.1.3) which is important for cognitive processes, including selective attention, planning, effortful regulation of affective states, error detection and monitoring of the environment. This system includes mainly the dorsal part of the anterior cingulate cortex as well as the dorsal and lateral part of the prefrontal cortex.

8.4 Conclusions and Outlook

In my opinion, both paradigms used in the present dissertation, namely the combination of emotional musical and visual stimuli and the non-interactive virtual reality environment, have proved to be useful for exploring the neural correlate of strong emotional experiences as well as the neural correlate of Spatial Presence, respectively. Moreover, similar networks were activated during the production as well as regulation of the emotional experiences in the virtual reality world as well as during listening and watching emotional stimuli.

Therefore, I think it would be promising to use the same paradigms in future studies to further explore the neural underpinnings of strong emotional experiences and Spatial Presence. For example, the roller coaster paradigm could be used in an fMRI study to elucidate the cortical as well as subcortical structures of Spatial Presence. Note that the Spatial Presence study of this dissertation has only revealed the cortical structures involved in the experience of Spatial Presence. However, there is still no study which explored the subcortical neural correlate of this fascinating phenomenon. Moreover, the cortical correlate of the Spatial Presence experience was explored in an arousing and non-interactive virtual reality world. Thus, future studies should also try to discover the neural correlate of Spatial Presence in interactive as well as less arousing virtual reality environments.

The neural correlate of strong emotional experiences was explored using fMRI and EEG and therefore both cortical as well as subcortical correlates could be elucidated. However, fMRI which revealed the cortical as well as subcortical correlates with high spatial resolution has a major disadvantage. That is the noisy scanner environment which can not be completely suppressed. Therefore, I suggest that it would be interesting and promising to explore the neural underpinnings of strong feelings using the same paradigm in a PET scanner. This method allows to measure cortical as well as subcortical structures in a silent environment and thus the emotional power of music can even be more effective in evoking strong feelings and experiences.

Not surprisingly, despite the remarkable and promising findings of this dissertation regarding the neural correlates of strong emotional experiences and Spatial Presence, there still remain many unanswered question, and there are numerous areas of uncertainty, where information is equivocal or lacking altogether. Nevertheless, I think and hope that the 3 discussed studies of this dissertation extended (at least a little bit) our knowledge of the *emotional, spatial* and maybe even *conscious* brain – one of the greatest, most fascinating and most complex mystery of the universe.

9 References

Aalto, S., Naatanen, P., Wallius, E., Metsahonkala, L., Stenman, H., Niem, P. M. et al. (2002). Neuroanatomical substrata of amusement and sadness: a PET activation study using film stimuli. *Neuroreport, 13,* 67-73.

Adam, J. J., Backes, W., Rijcken, J., Hofman, P., Kuipers, H., & Jolles, J. (2003). Rapid visuomotor preparation in the human brain: a functional MRI study. *Brain Res.Cogn Brain Res., 16,* 1-10.

Adolphs, R. (2002). Neural systems for recognizing emotion. *Curr.Opin.Neurobiol., 12,* 169-177.

Adolphs, R., Cahill, L., Schul, R., & Babinsky, R. (1997). Impaired declarative memory for emotional material following bilateral amygdala damage in humans. *Learn.Mem., 4,* 291-300.

Adolphs, R., Damasio, H., & Tranel, D. (2002). Neural systems for recognition of emotional prosody: a 3-D lesion study. *Emotion., 2,* 23-51.

Aftanas, L. I. & Golocheikine, S. A. (2002). Non-linear dynamic complexity of the human EEG during meditation. *Neurosci.Lett., 330,* 143-146.

Aicardi, J. (1998). The etiology of developmental delay. *Seminars In Pediatric Neurology, 5,* 15-20.

Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: role of the STS region. *Trends Cogn Sci., 4,* 267-278.

Altenmuller, E., Schurmann, K., Lim, V. K., & Parlitz, D. (2002). Hits to the left, flops to the right: different emotions during listening to music are reflected in cortical lateralisation patterns. *Neuropsychologia, 40,* 2242-2256.

Amassian, V. E., Cracco, R. Q., Maccabee, P. J., Cracco, J. B., Rudell, A. P., & Eberle, L. (1998). Transcranial magnetic stimulation in study of the visual pathway. *J Clin.Neurophysiol., 15,* 288-304.

Anders, S., Lotze, M., Erb, M., Grodd, W., & Birbaumer, N. (2004). Brain activity underlying emotional valence and arousal: A response-related fMRI study. *Hum.Brain Mapp., 23,* 200.

Anderson, A. K., Christoff, K., Panitz, D., De, R. E., & Gabrieli, J. D. (2003a). Neural correlates of the automatic processing of threat facial signals. *J.Neurosci., 23,* 5627-5633.

Anderson, A. K., Christoff, K., Stappen, I., Panitz, D., Ghahremani, D. G., Glover, G. et al. (2003b). Dissociated neural representations of intensity and valence in human olfaction. *Nat.Neurosci., 6,* 196-202.

Annett, M. (1970). A classification of hand preference by association analysis. *British Journal of Psychology, 61,* 303-321.

Asada, H., Fukuda, Y., Tsunoda, S., Yamaguchi, M., & Tonoike, M. (1999). Frontal midline theta rhythms reflect alternative activation of prefrontal cortex and anterior cingulate cortex in humans. *Neurosci.Lett., 274,* 29-32.

Ashburner, J. & Friston, K. J. (1999). Nonlinear spatial normalization using basis functions. *Hum.Brain Mapp., 7,* 254-266.

Band, G. P., van der Molen, M. W., Overtoom, C. C., & Verbaten, M. N. (2000). The ability to activate and inhibit speeded responses: separate developmental trends. *J.Exp.Child Psychol., 75,* 263-290.

Bard, P. (1929). The central representation of the sympathetic system: As indicated by certain physiological observations. *Archives of Neurology and Psychiatry, 22,* 230-246.

Bartels, A. & Zeki, S. (2000). The neural basis of romantic love. *Neuroreport, 11,* 3829-3834.

Bartels, A. & Zeki, S. (2004). Functional brain mapping during free viewing of natural scenes. *Hum.Brain Mapp., 21,* 75-85.

Beauchamp, M. S., Lee, K. E., Argall, B. D., & Martin, A. (2004). Integration of auditory and visual information about objects in superior temporal sulcus. *Neuron, 41,* 809-823.

Beauregard, M., Leroux, J. M., Bergman, S., Arzoumanian, Y., Beaudoin, G., Bourgouin, P. et al. (1998). The functional neuroanatomy of major depression: an fMRI study using an emotional activation paradigm. *Neuroreport, 9,* 3253-3258.

Bechara, A., Damasio, H., Tranel, D., & Anderson, S. W. (1998). Dissociation Of working memory from decision making within the human prefrontal cortex. *J.Neurosci., 18,* 428-437.

Berger, H. (1929). Über das Elektronencephalogramm des Menschen. *Archiv für Psychiatrie und Nervenkrankenheit, 87,* 527-570.

Binder, J. R., Frost, J. A., Hammeke, T. A., Bellgowan, P. S., Springer, J. A., Kaufman, J. N. et al. (2000). Human temporal lobe activation by speech and nonspeech sounds. *Cereb.Cortex, 10,* 512-528.

Biocca, F. (2001). Visual Touch in Virtual Environments: An Exploratory Study of Presence, Multimodal Interfaces, and Cross-Modal Sensory Illusions. *Presence: Teleoperators And Virtual Environments, 10,* 247-265.

Bischof, W. F. & Boulanger, P. (2003). Spatial navigation in virtual reality environments: an EEG analysis. *Cyberpsychol.Behav., 6,* 487-495.

Bjorklund, D. F. & Harnishfeger, K. K. (1990). The Resources Construct in Cognitive-Development - Diverse Sources of Evidence and A Theory of Inefficient Inhibition. *Developmental Review, 10,* 48-71.

Blair, R. J., Morris, J. S., Frith, C. D., Perrett, D. I., & Dolan, R. J. (1999). Dissociable neural responses to facial expressions of sadness and anger. *Brain, 122 (Pt 5),* 883-893.

Blanke, O., Landis, T., Spinelli, L., & Seeck, M. (2004). Out-of-body experience and autoscopy of neurological origin. *Brain, 127,* 243-258.

Blood, A. J. & Zatorre, R. J. (2001). Intensely pleasurable responses to music correlate with activity in brain regions implicated in reward and emotion. *Proc.Natl.Acad.Sci.U.S.A, 98,* 11818-11823.

Blood, A. J., Zatorre, R. J., Bermudez, P., & Evans, A. C. (1999). Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. *Nat.Neurosci., 2,* 382-387.

Bor, D., Duncan, J., Wiseman, R. J., & Owen, A. M. (2003). Encoding strategies dissociate prefrontal activity from working memory demand. *Neuron, 37,* 361-367.

Bördlein, I. & Kuschyk, J. (2004). Wenn das Herz rast beim Achterbahnfahren, liegt das an der Aufregung, nicht an der körperlichen Belastung. *Ärzte Zeitung-Online*.

Botvinick, M., Nystrom, L. E., Fissell, K., Carter, C. S., & Cohen, J. D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature, 402,* 179-181.

Braak, H., Braak, E., Yilmazer, D., & Bohl, J. (1996). Functional anatomy of human hippocampal formation and related structures. *J.Child Neurol., 11,* 265-275.

Breiter, H. C., Etcoff, N. L., Whalen, P. J., Kennedy, W. A., Rauch, S. L., Buckner, R. L. et al. (1996). Response and habituation of the human amygdala during visual processing of facial expression. *Neuron, 17,* 875-887.

Breiter, H. C., Gollub, R. L., Weisskoff, R. M., Kennedy, D. N., Makris, N., & Berke, J. D. (1997). Acute effects of cocaine on human brain activity and emotion. *Neuron, 19,* 591-611.

Brodmann, K. (1909). *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues*. Leipzig: Barth.

Brown, S., Martinez, M. J., & Parsons, L. M. (2004). Passive music listening spontaneously engages limbic and paralimbic systems. *Neuroreport, 15,* 2033-2037.

Buchel, C., Dolan, R. J., Armony, J. L., & Friston, K. J. (1999). Amygdala-hippocampal involvement in human aversive trace conditioning revealed through event-related functional magnetic resonance imaging. *J.Neurosci., 19,* 10869-10876.

Burgess, N., Jeffery, K. J., & O'Keefe, J. (1999). *The Hippocampal and Parietal Foundations of Spatial Cognition*. Oxford: University Press.

Bystrom, K.-E., Barfield, W., & Hendrix, C. (1999). A conceptual model of the sense of Presence in virtual environments. *Presence: Teleoperators And Virtual Environments, 8,* 241-244.

Cahill, L., Babinsky, R., Markowitsch, H. J., & McGaugh, J. L. (1995). The amygdala and emotional memory. *Nature, 377,* 295-296.

Calder, A. J., Lawrence, A. D., & Young, A. W. (2001). Neuropsychology of fear and loathing. *Nat.Rev.Neurosci., 2,* 352-363.

Calhoun, V. D., Pekar, J. J., McGinty, V. B., Adali, T., Watson, T. D., & Pearlson, G. D. (2002). Different activation dynamics in multiple neural systems during simulated driving. *Hum.Brain Mapp., 16,* 158-167.

Calhoun, V. D., Pekar, J. J., & Pearlson, G. D. (2004). Alcohol Intoxication Effects on Simulated Driving: Exploring Alcohol-Dose Effects on Brain Activation Using Functional MRI. *Neuropsychopharmacology*.

Calvert, G. A., Hansen, P. C., Iversen, S. D., & Brammer, M. J. (2001). Detection of audio-visual integration sites in humans by application of electrophysiological criteria to the BOLD effect. *Neuroimage., 14,* 427-438.

Canli, T., Zhao, Z., Brewer, J., Gabrieli, J. D., & Cahill, L. (2000). Event-related activation in the human amygdala associates with later memory for individual emotional experience. *J.Neurosci., 20,* RC99.

Cannon, W. B. (1927). The James-Lange theory of emotion: a critical examination and an alternative theory. *American Journal of Psychology, 39,* 106-124.

Carlson, L. A. (1999). Selecting a reference frame. *Spatial Cognition and Computation, 1,* 365-379.

Carretie, L., Hinojosa, J. A., Martin-Loeches, M., Mercado, F., & Tapia, M. (2004). Automatic attention to emotional stimuli: neural correlates. *Hum.Brain Mapp., 22,* 290-299.

Carretie, L., Mercado, F., Tapia, M., & Hinojosa, J. A. (2001). Emotion, attention, and the 'negativity bias', studied through event-related potentials. *Int.J.Psychophysiol., 41,* 75-85.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science, 280,* 747-749.

Caton, R. (1875). The electric currents of the brain. *British Medical Journal, 2,* 278.

Chouinard, S., Briere, M. E., Rainville, C., & Godbout, R. (2003). Correlation between evening and morning waking EEG and spatial orientation. *Brain Cogn, 53,* 162-165.

Cohen, J. (1969). *Statistical power analysis for the behavioral sciences.* New York: Academic Press.

Cooke, D. (1959). *The language of music*. Oxford: University Press.

Corballis, M. C. (1991). *The lopsided ape*. New York, Oxford: Oxford University Press.

Corballis, M. C. (1992). On the evolution of language and generativity. *Cognition, 44,* 197-126.

Corbetta, M. & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nat.Rev.Neurosci., 3,* 201-215.

Craig, A. D. (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nat.Rev.Neurosci., 3,* 655-666.

Cunningham, J. G. & Sterling, R. S. (1988). Developmental changes in the understanding of affective meaning in music. *Motivation and Emotion, **12**,* 399-412.

Cupchick, C. C., Rickert, M., & Mendelson, J. (1982). Similarity and preference judgements of muscial stimuli. *Scandinavian Journal of Psychology, 23,* 273-282.

Daffner, K. R., Mesulam, M. M., Holcomb, P. J., Calvo, V., Acar, D., Chabrerie, A. et al. (2000a). Disruption of attention to novel events after frontal lobe injury in humans. *J.Neurol.Neurosurg.Psychiatry, 68,* 18-24.

Daffner, K. R., Mesulam, M. M., Scinto, L. F., Acar, D., Calvo, V., Faust, R. et al. (2000b). The central role of the prefrontal cortex in directing attention to novel events. *Brain, 123 (Pt 5),* 927-939.

Damasio, A. R. (1994). Descartes' error and the future of human life. *Sci.Am., 271,* 144.

Damasio, A. R., Grabowski, T. J., Bechara, A., Damasio, H., Ponto, L. L., Parvizi, J. et al. (2000). Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nat.Neurosci., 3,* 1049-1056.

Davidson, R. J. (2003). Affective neuroscience and psychophysiology: toward a synthesis. *Psychophysiology, 40,* 655-665.

Davidson, R. J. & Hugdahl, K. (1996). Baseline asymmetries in brain electrical activity predict dichotic listening performance. *Neuropsychology, 10,* 241-246.

Davidson, R. J. & Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. *Trends Cogn Sci., 3,* 11-21.

Davidson, R. J., Jackson, D. C., & Kalin, N. H. (2000). Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. *Psychol.Bull., 126,* 890-909.

Davidson, R. J., Schwartz, G. E., Saron, C., Bennett, J., & Goleman, D. J. (1979). Frontal versus parietal EEG asymmetry during positive and negative affect. *Psychophysiology, 16,* 202-203.

Davis, M. & Whalen, P. J. (2001). The amygdala: vigilance and emotion. *Mol.Psychiatry, 6,* 13-34.

De Araujo, D. B., Baffa, O., & Wakai, R. T. (2001). Theta and alpha oscillations: Dependency on navigation tasks. In J.Nenonen, R. J. Ilmoniemi, & T. Katila (Eds.), *Biomag2000. Proceedings of the 12th International Conference on Biomagnetism, Helskinki University of Technology* (pp. 343-346). Finland: Espoo.

de Gelder, B. & Vroomen, J. (2000). The perception of emotions by ear and by eye. *Cognition & Emotion, 14,* 289-311.

Decety, J. & Chaminade, T. (2003). Neural correlates of feeling sympathy. *Neuropsychologia, 41,* 127-138.

Dehaene, S., Naccache, L., Cohen, L., Bihan, D. L., Mangin, J. F., Poline, J. B. et al. (2001). Cerebral mechanisms of word masking and unconscious repetition priming. *Nat.Neurosci., 4,* 752-758.

Devan, B. D. & White, N. M. (1999). Parallel information processing in the dorsal striatum: relation to hippocampal function. *J.Neurosci., 19,* 2789-2798.

Dickson, J., Drury, H., & Van Essen, D. C. (2001). 'The surface management system' (SuMS) database: a surface-based database to aid cortical surface reconstruction, visualization and analysis. *Philos.Trans.R.Soc.Lond B Biol.Sci., 356,* 1277-1292.

Dinh, H. Q., Walker, N., & Hodges, L. F. (1999). Evaluating the Importance of Mulit-sensory Input on Memory and the Sense of Presence in Virtual Environments. In *Proceedings of Virtual Reality '99* (pp. 222-228). Los Alamitos: IEEE.

Dolan, R. J., Morris, J. S., & de, G. B. (2001). Crossmodal binding of fear in voice and face. *Proc.Natl.Acad.Sci.U.S.A, 98,* 10006-10010.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron, 42,* 855-863.

Downar, J., Crawley, A. P., Mikulis, D. J., & Davis, K. D. (2000). A multimodal cortical network for the detection of changes in the sensory environment. *Nat.Neurosci., 3,* 277-283.

Dupont, S. (2002). Investigating temporal pole function by functional imaging. *Epileptic.Disord., 4 Suppl 1,* S17-S22.

Ekman, P. (1999). Basic Emotions. In T.Dalgleish & M. Power (Eds.), *Handbook of Cognition and Emotion* (pp. 45-60). Chichester, England: Wiley.

Ekman, P. & Friesen, W. V. (1976). *Pictures of facial effect*. Palo Alto: Consulting Psychologists.

Elliott, R., Friston, K. J., & Dolan, R. J. (2000). Dissociable neural responses in human reward systems. *J.Neurosci., 20,* 6159-6165.

Esslen, M., Pascual-Marqui, R. D., Hell, D., Kochi, K., & Lehmann, D. (2004). Brain areas and time course of emotional processing. *Neuroimage., 21,* 1189-1203.

Fernandez, E., Alfaro, A., Tormos, J. M., Climent, R., Martinez, M., Vilanova, H. et al. (2002). Mapping of the human visual cortex using image-guided transcranial magnetic stimulation. *Brain Res.Brain Res.Protoc., 10,* 115-124.

Flanagan, P., McAnally, K. I., Martin, R. L., Meehan, J. W., & Oldfield, S. R. (1998). Aurally and visually guided visual search in a virtual environment. *Hum.Factors, 40,* 461-468.

Freeman, J., Avons, S. E., Pearson, D. E., & Ijsselsteijn, W. A. (1999). Effects of sensory information and prior experience on direct subjective ratings of presence. *Presence: Teleoperators And Virtual Environments, 8,* 1-13.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J., Frith, C. D., & Frackowiak, R. S. (1995). Statistical Parametric Maps in functional imaging: A general linear approach. *Hum.Brain Mapp., 2,* 189-210.

Friston, K. J., Josephs, O., Zarahn, E., Holmes, A. P., Rouquette, S., & Poline, J. (2000). To smooth or not to smooth? Bias and efficiency in fMRI time-series analysis. *Neuroimage., 12,* 196-208.

Friston, K. J., Price, C. J., Buechel, C., & Franckowiak, R. S. J. (1997). A taxonomy of study design. In R.S.J.Franckowiak, K. J. Friston, C. D. Frith, R. J. Dolan, & J. C. Mazziotta (Eds.), *Human brain function* (pp. 141-159). San Diego: Academic Press.

Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S., & Turner, R. (1996). Movement-related effects in fMRI time-series. *Magn Reson.Med., 35,* 346-355.

Fuster, J. M. (2002). Frontal lobe and cognitive development. *J.Neurocytol., 31,* 373-385.

Gabrielsson, A. & Juslin, P. N. (1996). Emotional expression in music performance: between the performer's intention and the listener's experience. *Psychology of Music, 24,* 68-91.

Gamma, A., Lehmann, D., Frei, E., Iwata, K., Pascual-Marqui, R. D., & Vollenweider, F. X. (2004). Comparison of simultaneously recorded [H2(15)O]-PET and LORETA during cognitive and pharmacological activation. *Hum.Brain Mapp., 22,* 83-96.

Garavan, H., Pendergrass, J. C., Ross, T. J., Stein, E. A., & Risinger, R. C. (2001). Amygdala response to both positively and negatively valenced stimuli. *Neuroreport, 12,* 2779-2783.

George, M. S., Ketter, T. A., Parekh, P. I., Herscovitch, P., & Post, R. M. (1996). Gender differences in regional cerebral blood flow during transient self-induced sadness or happiness. *Biol.Psychiatry, 40,* 859-871.

Giedd, J. N. (2004). Structural magnetic resonance imaging of the adolescent brain. *Ann.N.Y.Acad.Sci., 1021,* 77-85.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A. et al. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Nat.Neurosci., 2,* 861-863.

Glascher, J., Tuscher, O., Weiller, C., & Buchel, C. (2004). Elevated responses to constant facial emotions in different faces in the human amygdala: an fMRI study of facial identity and expression. *BMC.Neurosci., 5,* 45.

Goldman, R. I., Stern, J. M., Engel, J., Jr., & Cohen, M. S. (2002). Simultaneous EEG and fMRI of the alpha rhythm. *Neuroreport, 13,* 2487-2492.

Gordon, E. (1999). Brain imaging technologies: how, what, when and why? *Australien and New Zealand Journal of Psychiatry, 33,* 187-196.

Gottfried, J. A., O'Doherty, J., & Dolan, R. J. (2002). Appetitive and aversive olfactory learning in humans studied using event-related functional magnetic resonance imaging. *J.Neurosci., 22,* 10829-10837.

Griffiths, T. D. (2000). Musical hallucinosis in acquired deafness. Phenomenology and brain substrate. *Brain, 123 (Pt 10),* 2065-2076.

Gron, G., Wunderlich, A. P., Spitzer, M., Tomczak, R., & Riepe, M. W. (2000). Brain activation during human navigation: gender-different neural networks as substrate of performance. *Nat.Neurosci., 3,* 404-408.

Gur, R. C., Schroeder, L., Turner, T., McGrath, C., Chan, R. M., Turetsky, B. I. et al. (2002). Brain activation during facial emotion processing. *Neuroimage., 16,* 651-662.

Gusnard, D. A., Akbudak, E., Shulman, G. L., & Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc.Natl.Acad.Sci.U.S.A, 98,* 4259-4264.

Haalman, I. & Vaadia, E. (1997). Dynamics of neuronal interactions: relation to behavior firing rates, and distance between neurons. *Human brain mapping, 5,* 249-253.

Hamann, S. & Mao, H. (2002). Positive and negative emotional verbal stimuli elicit activity in the left amygdala. *Neuroreport, 13,* 15-19.

Hamann, S. B., Ely, T. D., Grafton, S. T., & Kilts, C. D. (1999). Amygdala activity related to enhanced memory for pleasant and aversive stimuli. *Nat.Neurosci., 2,* 289-293.

Hariri, A. R., Bookheimer, S. Y., & Mazziotta, J. C. (2000). Modulating emotional responses: effects of a neocortical network on the limbic system. *Neuroreport, 11,* 43-48.

Hariri, A. R., Tessitore, A., Mattay, V. S., Fera, F., & Weinberger, D. R. (2002). The amygdala response to emotional stimuli: a comparison of faces and scenes. *Neuroimage., 17,* 317-323.

Harris, S. R., Kemmerling, R. L., & North, M. M. (2002). Brief virtual reality therapy for public speaking anxiety. *Cyberpsychol.Behav., 5,* 543-550.

Hebert, R. & Lehmann, D. (1977). Theta bursts: an EEG pattern in normal subjects practising the transcendental meditation technique. *Electroencephalogr.Clin.Neurophysiol., 42,* 397-405.

Heeger, D. J. & Ress, D. (2002). What does fMRI tell us about neuronal activity? *Nat.Rev.Neurosci., 3,* 142-151.

Heeter, C. (1992). Being there: The subjective experience of presence. *Presence: Teleoperators And Virtual Environments, 1,* 262-271.

Heilman, K. M. & Valenstein, E. (2003). *Clinical Neuropsychology*. New York: Oxford University Press.

Hein, A. & Held, R. (1962). A neural model for labile sensorimotor coordinations. In E.E.Bernstein & M. R. Kare (Eds.), *Biological Prototypes and Synthetic Systems 1* (New York: Plenum Press.

Heller, W., Nitschke, J. B., Etienne, M. A., & Miller, G. A. (1997). Patterns of regional brain activity differentiate types of anxiety. *J.Abnorm.Psychol., 106,* 376-385.

Henderson, C. J., Butler, S. R., & Glass, A. (1975). The localization of equivalent dipoles of EEG sources by the application of electrical field theory. *Electroencephalography and Clinical Neurophysiology, 39,* 117-130.

Hendrix, C. & Barfield, W. (1996). Presence within virtual environments as a function of visual display parameters. *Presence: Teleoperators And Virtual Environments, 5,* 274-289.

Hevner, K. (1936). Experimental studies of the elements of expression in music. *American Journal of Psychology, 48,* 246-268.

Heyder, K., Suchan, B., & Daum, I. (2004). Cortico-subcortical contributions to executive control. *Acta Psychol.(Amst), 115,* 271-289.

Hickok, G. & Poeppel, D. (2000). Towards a functional neuroanatomy of speech perception. *Trends Cogn Sci., 4,* 131-138.

Hoffman, H. G., Prothero, J., Wells, M. J., & Groen, J. (1998). Virtual chess: meaning enhances users' sense of presence in virtual environments. *International Journal of Human-Computer Interaction, 10,* 251-263.

Hoffman, H. G., Richards, T. L., Magula, J., Seibel, E. J., Hayes, C., Mathis, M. et al. (2003). A magnet-friendly virtual reality fiberoptic image delivery system. *Cyberpsychol.Behav., 6,* 645-648.

Holm, S. (1979). A simple sequentially rejective multiple test procedure. *Scandinavian Journal of Statistic, 6,* 65-70.

Holmes, A. P., Blair, R. C., Watson, J. D. G., & Ford, I. (1996). Nonparametric analysis of statistic images from functional mapping experiments. *J Cereb Blood Flow Metab, 16,* 7-22.

Huang, M. P. & Alessi, N. E. (1999). Presence as an emotional experience. *Stud.Health Technol.Inform., 62:148-53.,* 148-153.

Huang, M. P. & Alessi, N. E. (1998). Mental health implications for presence. *Cyberpsychol.Behav., 2,* 15-18.

Ijsselsteijn, W. A. (2002). Elements of a multi-level theory of presence: Phenomenology, mental processing and neural correlates. *Proceedings of Presence,* 245-259.

Ijsselsteijn, W. A., de Ridder, H., Freeman, J., Avons, S. E., & Bouwhuis, D. (2001). Effects of Stereoscopic Presentation, Image Motion, and Screen Size on Subjective and Objective Corroborative Measures of Presence. *Presence, 10,* 298-311.

Ijsselsteijn, W. A., de Ridder, H., Hamberg, R., Bouwhuis, D., & Freeman, J. (1998). Perceived depth and the feeling of presence in 3DTV. *Displays, 18,* 207-214.

Ishii, R., Shinosaki, K., Ukai, S., Inouye, T., Ishihara, T., Yoshimine, T. et al. (1999). Medial prefrontal cortex generates frontal midline theta rhythm. *Neuroreport, 10,* 675-679.

Izard, Dougherty, Bloxom, & Kotosch (1974). *Differential Emotions Scale*.

James, W. (1884). What is an emotion? *Mind, 9,* 188-206.

Jancke, L. (2005). Introducing the concept of Spatial Presence. A neuroscientific approach. *Neuroreport, submitted article*.

Jäncke, L. (2005). *Methoden der Bildgebung in der Psychologie und den kognitiven Neurowissenschaften*. Stuttgart: Kohlhammer.

Jancke, L., Loose, R., Lutz, K., Specht, K., & Shah, N. J. (2000). Cortical activations during paced finger-tapping applying visual and auditory pacing stimuli. *Brain Res.Cogn Brain Res., 10,* 51-66.

Jancke, L. & Shah, N. J. (2002). Does dichotic listening probe temporal lobe functions? *Neurology, 58,* 736-743.

Jancke, L., Wustenberg, T., Scheich, H., & Heinze, H. J. (2002). Phonetic perception and the temporal cortex. *Neuroimage., 15,* 733-746.

Jasper, H. (1958). The ten twenty electrode system of the International Federation. *Electroencephalography and Clinical Neurophysiology, 10,* 371-375.

Jordan, K., Heinze, H. J., Lutz, K., Kanowski, M., & Jancke, L. (2001). Cortical activations during the mental rotation of different visual objects. *Neuroimage., 13,* 143-152.

Jordan, K., Schadow, J., Wuestenberg, T., Heinze, H. J., & Jancke, L. (2004). Different cortical activations for subjects using allocentric or egocentric strategies in a virtual navigation task. *Neuroreport, 15,* 135-140.

Jordan, K., Wustenberg, T., Heinze, H. J., Peters, M., & Jancke, L. (2002). Women and men exhibit different cortical activation patterns during mental rotation tasks. *Neuropsychologia, 40,* 2397-2408.

Kahana, M. J., Sekuler, R., Caplan, J. B., Kirschen, M., & Madsen, J. R. (1999). Human theta oscillations exhibit task dependence during virtual maze navigation. *Nature, 399,* 781-784.

Kavanagh, R. N., Darcey, R. M., Lehmann, D., & Fender, D. H. (1978). Evaluation of methods for three-dimensional localization of electrical sources in the human brain. *IEEE Transactions on Biomedical Engineering, 25,* 421-429.

Khalfa, S., Isabelle, P., Jean-Pierre, B., & Manon, R. (2002). Event-related skin conductance responses to musical emotions in humans. *Neurosci.Lett., 328,* 145-149.

Kimbrell, T. A., George, M. S., Parekh, P. I., Ketter, T. A., Podell, D. M., Danielson, A. L. et al. (1999). Regional brain activity during transient self-induced anxiety and anger in healthy adults. *Biol.Psychiatry, 46,* 454-465.

Kjaer, T. W., Bertelsen, C., Piccini, P., Brooks, D., Alving, J., & Lou, H. C. (2002). Increased dopamine tone during meditation-induced change of consciousness. *Brain Res.Cogn Brain Res., 13,* 255-259.

Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Res.Brain Res.Rev., 29,* 169-195.

Klimmt, C. & Vorderer, P. (2003). Media Psychology "is not yet there": Introducing theories on media entertainment to the Presence debate. *Presence: Teleoperators And Virtual Environments, 12,* 346-359.

Knight, R. T. & Scabini, D. (1998). Anatomic bases of event-related potentials and their relationship to novelty detection in humans. *J.Clin.Neurophysiol., 15,* 3-13.

Knutson, B., Fong, G. W., Adams, C. M., Varner, J. L., & Hommer, D. (2001). Dissociation of reward anticipation and outcome with event-related fMRI. *Neuroreport, 12,* 3683-3687.

Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain, 122 (Pt 5),* 981-991.

Krolak-Salmon, P., Henaff, M. A., Vighetto, A., Bertrand, O., & Mauguiere, F. (2004). Early amygdala reaction to fear spreading in occipital, temporal, and frontal cortex: a depth electrode ERP study in human. *Neuron, 42,* 665-676.

Krumhansl, C. L. (1997). An exploratory study of musical emotions and psychophysiology. *Can.J.Exp.Psychol., 51,* 336-353.

Kubicki, S., Herrmann, W. M., Fichte, K., & Freund, G. (1979). Reflections on the topics: EEG frequency bands and regulation of vigilance. *Pharmakopsychiatr.Neuropsychopharmakol., 12,* 237-245.

Laarni, J., Ravaja, N., & Saari, T. (2004). Measuring mental workload, presence and situation awareness in synthetic environements by eye tracking and psychophysiological methods. Proceedings of WWCS .
Ref Type: Unpublished Work

Lane, R. D., Reiman, E. M., Ahern, G. L., Schwartz, G. E., & Davidson, R. J. (1997). Neuroanatomical correlates of happiness, sadness, and disgust. *Am.J.Psychiatry, 154,* 926-933.

Lang, P. J., Bradley, M., & Cuthbert, B. International Affective Picture System. 1995. Gainsville, Florida, Center for Research in Psychophysiology.

Lang, P. J., Bradley, M. M., Fitzsimmons, J. R., Cuthbert, B. N., Scott, J. D., Moulder, B. et al. (1998). Emotional arousal and activation of the visual cortex: an fMRI analysis. *Psychophysiology, 35,* 199-210.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology, 30,* 261-273.

Lange, C. (1885). *Die Gemütsbewegungen*. Würzburg: Kabitsch.

Larson, C. L., Davidson, R. J., Abercrombie, H. C., Ward, R. T., Schaefer, S. M., Jackson, D. C. et al. (1998). Relations between PET-derived measures of thalamic glucose metabolism and EEG alpha power. *Psychophysiology, 35,* 162-169.

Larsson, P., Vastfjall, D., & Kleiner, M. (2001). The actor-observer effect in virtual reality presentations. *Cyberpsychol.Behav., 4,* 239-246.

Laufs, H., Kleinschmidt, A., Beyerle, A., Eger, E., Salek-Haddadi, A., Preibisch, C. et al. (2003a). EEG-correlated fMRI of human alpha activity. *Neuroimage., 19,* 1463-1476.

Laufs, H., Krakow, K., Sterzer, P., Eger, E., Beyerle, A., Salek-Haddadi, A. et al. (2003b). Electroencephalographic signatures of attentional and cognitive default modes in spontaneous brain activity fluctuations at rest. *Proc.Natl.Acad.Sci.U.S.A, 100,* 11053-11058.

Laux, L., Glanzmann, P., Schaffner, P., & Spielberger, C. D. (1981). *Das State-Trait-Angstinventar: Theoretische Grundlagen und Handanweisungen*. Weinheim: Beltz.

Lee, G. P., Meador, K. J., Loring, D. W., Allison, J. D., Brown, W. S., Paul, L. K. et al. (2004). Neural substrates of emotion as revealed by functional magnetic resonance imaging. *Cogn Behav.Neurol., 17,* 9-17.

Lehmann, D. (1988). The view of an EEG-EP mapper. *Brain Topogr., 1,* 77-78.

Lehmann, D. (1990). Past, present and future of topographic mapping. *Brain Topogr., 3,* 191-202.

Lehmann, D., Kavanagh, R. N., & Fender, D. H. (1969). Field studies of averaged visually evoked EEG potentials in a patient with a split chiasm. *Journal of Electroencephalography and Clinical Neurophysiology, 26,* 193-199.

Lehmann, D. & Skrandies, W. (1980). Reference-free identification of components of checkerboard-evoked multichannel potential fields. *Electroencephalography and Clinical Neurophysiology, 48,* 609-621.

Lessiter, J., Freeman, J., Keogh, E., & Davidoff, J. (2001). A Cross-Media Presence Questionnaire: The ITC-Sense of Presence Inventory. *Presence, 10,* 282-297.

Liotti, M., Mayberg, H. S., Brannan, S. K., McGinnis, S., Jerabek, P., & Fox, P. T. (2000). Differential limbic--cortical correlates of sadness and anxiety in healthy subjects: implications for affective disorders. *Biol.Psychiatry, 48,* 30-42.

Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature, 412,* 150-157.

Lombard, M. & Ditton, T. (1997). At the heart of it all: the concept of Presence. *Journal of Computer-mediated Communication, 3,* http://www.ascusc.org/jcmc/vol3/issue2/lombard.html.

Lorenz, J., Minoshima, S., & Casey, K. L. (2003). Keeping pain out of mind: the role of the dorsolateral prefrontal cortex in pain modulation. *Brain, 126,* 1079-1091.

Luna, B., Thulborn, K. R., Munoz, D. P., Merriam, E. P., Garver, K. E., Minshew, N. J. et al. (2001). Maturation of widely distributed brain function subserves cognitive development. *Neuroimage., 13,* 786-793.

Lutz, K., Specht, K., Shah, N. J., & Jancke, L. (2000). Tapping movements according to regular and irregular visual timing signals investigated with fMRI. *Neuroreport, 11,* 1301-1306.

Maddock, R. J. & Buonocore, M. H. (1997). Activation of left posterior cingulate gyrus by the auditory presentation of threat-related words: an fMRI study. *Psychiatry Res., 75,* 1-14.

Maddock, R. J., Garrett, A. S., & Buonocore, M. H. (2003). Posterior cingulate cortex activation by emotional words: fMRI evidence from a valence decision task. *Hum.Brain Mapp., 18,* 30-41.

Maguire, E. A., Burgess, N., Donnett, J. G., Frackowiak, R. S. J., Frith, C. D., & O'Keefe, J. (1998). Knowing Where an Getting There: A Human Navigation Network. *Science, 280,* 921-924.

Maguire, E. A. & Mummery, C. J. (1999). Differential modulation of a common memory retrieval network revealed by positron emission tomography. *Hippocampus, 9,* 54-61.

Mania, K. & Chalmers, A. (2001). The effects of levels of immersion on memory and presence in virtual environments: a reality centered approach. *Cyberpsychol.Behav., 4,* 247-264.

Massaro, D. W. & Egan, P. B. (1996). Perceiving affect from the voice and the face. *Psychonomic Bulletin & Review, 3,* 215-221.

Mayberg, H. S., Liotti, M., Brannan, S. K., McGinnis, S., Mahurin, R. K., & Jerabek, P. A. (1999). Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. *Am.J.Psychiatry, 156,* 675-682.

McGaugh, J. L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annu.Rev.Neurosci., 27,* 1-28.

Meehan, M. (2001). *Physiological Reaction as an Objective Measure of Presence.* University of North Carolina, Chapel Hill, USA.

Meehan, M., Insko, B., Whitton, M., & Brooks, F. P. (2002). Physiological measures of presence in stressful virtual environments. *Acm Transactions on Graphics, 21,* 645-652.

Mellet, E., Bricogne, S., Tzourio, N., Ghaem, O., Petit, L., Zago, L. et al. (2000). Neural Correlates of Topographic Mental Exploration: The Impact of Route versus Survey Perspective Learning. *Neuroimage., 12,* 588-600.

Menon, V., Adleman, N. E., White, C. D., Glover, G. H., & Reiss, A. L. (2001). Error-related brain activation during a Go/NoGo response inhibition task. *Hum.Brain Mapp., 12,* 131-143.

Mesulam, M. M. (1998). From sensation to cognition. *Brain, 121 (Pt 6),* 1013-1052.

Mesulam, M. M., Nobre, A. C., Kim, Y. H., Parrish, T. B., & Gitelman, D. R. (2001). Heterogeneity of cingulate contributions to spatial attention. *Neuroimage., 13,* 1065-1072.

Mineka, S. & Ohman, A. (2002). Phobias and preparedness: the selective, automatic, and encapsulated nature of fear. *Biol.Psychiatry, 52,* 927-937.

Moran, J. M., Wig, G. S., Adams, R. B., Jr., Janata, P., & Kelley, W. M. (2004). Neural correlates of humor detection and appreciation. *Neuroimage., 21,* 1055-1060.

Morris, J. S., Friston, K. J., Buchel, C., Frith, C. D., Young, A. W., Calder, A. J. et al. (1998). A neuromodulatory role for the human amygdala in processing emotional facial expressions. *Brain, 121 (Pt 1),* 47-57.

Morris, J. S., Frith, C. D., Perrett, D. I., Rowland, D., Young, A. W., Calder, A. J. et al. (1996). A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature, 383,* 812-815.

Morris, R., Pandya, D. N., & Petrides, M. (1999). Fiber system linking the mid-dorsolateral frontal cortex with the retrosplenial/presubicular region in the rhesus monkey. *J.Comp Neurol., 407,* 183-192.

Moutoussis, K. & Zeki, S. (2002). The relationship between cortical activation and perception investigated with invisible stimuli. *Proc.Natl.Acad.Sci.U.S.A, 99,* 9527-9532.

Mraz, R., Hong, J., Quintin, G., Staines, W. R., McIlroy, W. E., Zakzanis, K. K. et al. (2003). A platform for combining virtual reality experiments with functional magnetic resonance imaging. *Cyberpsychol.Behav., 6,* 359-368.

Nakahara, K., Hayashi, T., Konishi, S., & Miyashita, Y. (2002). Functional MRI of macaque monkeys performing a cognitive set-shifting task. *Science, 295,* 1532-1536.

Nakamura, K., Kawashima, R., Ito, K., Sugiura, M., Kato, T., Nakamura, A. et al. (1999). Activation of the right inferior frontal cortex during assessment of facial emotion. *J.Neurophysiol., 82,* 1610-1614.

Noesselt, T., Shah, N. J., & Jancke, L. (2003). Top-down and bottom-up modulation of language related areas - An fMRI Study. *BMC Neurosci., 4,* 13.

Nordenstreng, K. (1968). A comparison between the semantic differential and similarity analysis in the measurement of musical experience. *Scandinavian Journal of Psychology, 9,* 89-96.

Northoff, G., Richter, A., Gessner, M., Schlagenhauf, F., Fell, J., Baumgart, F. et al. (2000). Functional dissociation between medial and lateral prefrontal cortical spatiotemporal activation in negative and positive emotions: a combined fMRI/MEG study. *Cereb.Cortex, 10,* 93-107.

Nunez, P. L. (1981). *Electrical fields of the brain*. New York: Oxford University Press.

O'Brien, R. G. & Kaiser, M. K. (1985). MANOVA method for analyzing repeated measures designs: an extensive primer. *Psychological Bulletin, 97,* 316-333.

O'Doherty, J., Kringelbach, M. L., Rolls, E. T., Hornak, J., & Andrews, C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. *Nat.Neurosci., 4,* 95-102.

O'Keefe, J. & Recce, M. L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus, 3,* 317-330.

Oakes, T. R., Pizzagalli, D. A., Hendrick, A. M., Horras, K. A., Larson, C. L., Abercrombie, H. C. et al. (2004). Functional coupling of simultaneous electrical and metabolic activity in the human brain. *Hum.Brain Mapp., 21,* 257-270.

Ohman, A. & Mineka, S. (2001). Fears, phobias, and preparedness: toward an evolved module of fear and fear learning. *Psychol.Rev., 108,* 483-522.

Ohnishi, T., Matsuda, H., Asada, T., Aruga, M., Hirakata, M., Nishikawa, M. et al. (2001). Functional anatomy of musical perception in musicians. *Cereb.Cortex, 11,* 754-760.

Olds, J. & Milner, P. (1954). Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *J Comp Physiol Psychol, 47,* 419-426.

Owen, A. M. (1997). The functional organization of working memory processes within human lateral frontal cortex: the contribution of functional neuroimaging. *Eur.J.Neurosci., 9,* 1329-1339.

Packard, M. G. (1999). Glutamate infused posttraining into the hippocampus or caudate-putamen differentially strengthens place and response learning. *Proc.Natl.Acad.Sci.U.S.A, 96,* 12881-12886.

Packard, M. G. & Cahill, L. (2001). Affective modulation of multiple memory systems. *Curr.Opin.Neurobiol., 11,* 752-756.

Pagnoni, G., Zink, C. F., Montague, P. R., & Berns, G. S. (2002). Activity in human ventral striatum locked to errors of reward prediction. *Nat.Neurosci., 5,* 97-98.

Pascual-Marqui, R. D. (1999). Review of Methods for Solving the EEG Inverse Problem. *International Journal of Bioelectromagnetism, 1,* 75-86.

Pascual-Marqui, R. D., Esslen, M., Kochi, K., & Lehmann, D. (2002). Functional imaging with low-resolution brain electromagnetic tomography (LORETA): a review. *Methods Find.Exp.Clin.Pharmacol., 24 Suppl C,* 91-95.

Pascual-Marqui, R. D., Lehmann, D., Koenig, T., Kochi, K., Merlo, M. C., Hell, D. et al. (1999). Low resolution brain electromagnetic tomography (LORETA) functional imaging in acute, neuroleptic-naive, first-episode, productive schizophrenia. *Psychiatry Res., 90,* 169-179.

Pascual-Marqui, R. D., Michel, C. M., & Lehmann, D. (1994). Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *Int.J.Psychophysiol., 18,* 49-65.

Paus, T., Koski, L., Caramanos, Z., & Westbury, C. (1998). Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: a review of 107 PET activation studies. *Neuroreport, 9,* R37-R47.

Penhune, V. B., Zattore, R. J., & Evans, A. C. (1998). Cerebellar contributions to motor timing: a PET study of auditory and visual rhythm reproduction. *J.Cogn Neurosci., 10,* 752-765.

Peretz, I. (2001). Listen to the brain: The biological perspective on musical emotions. In P.Juslin & J. Sloboda (Eds.), *Music and Emotion: Theory and Research* (pp. 105-134). Oxford: University Press.

Peretz, I., Gagnon, L., & Bouchard, B. (1998). Music and emotion: perceptual determinants, immediacy, and isolation after brain damage. *Cognition, 68,* 111-141.

Pessoa, L., McKenna, M., Gutierrez, E., & Ungerleider, L. G. (2002). Neural processing of emotional faces requires attention. *Proc.Natl.Acad.Sci.U.S.A, 99,* 11458-11463.

Petrides, M. (1994). Frontal lobes and behaviour. *Curr.Opin.Neurobiol., 4,* 207-211.

Pfurtscheller, G. (1992). Event-related synchronization (ERS): an electrophysiological correlate of cortical areas at rest. *Electroencephalogr.Clin.Neurophysiol., 83,* 62-69.

Pfurtscheller, G. (1989). Spatiotemporal analysis of alpha frequency components with the ERD technique. *Brain Topogr., 2,* 3-8.

Pfurtscheller, G. & Aranibar, A. (1977). Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalogr.Clin.Neurophysiol., 42,* 817-826.

Pfurtscheller, G., Stancak, A., Jr., & Neuper, C. (1996). Event-related synchronization (ERS) in the alpha band--an electrophysiological correlate of cortical idling: a review. *Int.J.Psychophysiol., 24,* 39-46.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage., 16,* 331-348.

Phillips, M. L., Drevets, W. C., Rauch, S. L., & Lane, R. (2003). Neurobiology of emotion perception I: The neural basis of normal emotion perception. *Biol.Psychiatry, 54,* 504-514.

Phillips, M. L., Young, A. W., Scott, S. K., Calder, A. J., Andrew, C., Giampietro, V. et al. (1998). Neural responses to facial and vocal expressions of fear and disgust. *Proc.R.Soc.Lond B Biol.Sci., 265,* 1809-1817.

Phillips, M. L., Young, A. W., Senior, C., Brammer, M., Andrew, C., Calder, A. J. et al. (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature, 389,* 495-498.

Ploghaus, A., Tracey, I., Gati, J. S., Clare, S., Menon, R. S., Matthews, P. M. et al. (1999). Dissociating pain from its anticipation in the human brain. *Science, 284,* 1979-1981.

Pourtois, G., de, G. B., Bol, A., & Crommelinck, M. (2005). Perception of facial expressions and voices and of their combination in the human brain. *Cortex, 41,* 49-59.

Pruessmann, K. P., Weiger, M., Scheidegger, M. B., & Boesiger, P. (1999). SENSE: sensitivity encoding for fast MRI. *Magn Reson.Med., 42,* 952-962.

Psotka, J. (1995). Immersive training systems: Virtual reality and education and training. *Instructional Science, 23,* 405-431.

Pujol, J., Lopez-Sala, A., Sebastian-Galles, N., Deus, J., Cardoner, N., Soriano-Mas, C. et al. (2004). Delayed myelination in children with developmental delay detected by volumetric MRI. *Neuroimage., 22,* 897-903.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proc.Natl.Acad.Sci.U.S.A, 98,* 676-682.

Rauch, S. L., Shin, L. M., Dougherty, D. D., Alpert, N. M., Orr, S. P., Lasko, M. et al. (1999). Neural activation during sexual and competitive arousal in healthy men. *Psychiatry Res., 91,* 1-10.

Reiman, E. M., Lane, R. D., Ahern, G. L., Schwartz, G. E., Davidson, R. J., & Friston, K. J. (1997). Neuroanatomical correlates of externally and internally generated human emotion. *Am.J.Psychiatry, 154,* 918-925.

Ridderinkhof, K. R. & Vandermolen, M. W. (1995). A Psychophysiological Analysis of Developmental Differences in the Ability to Resist Interference. *Child Development, 66,* 1040-1056.

Robillard, G., Bouchard, S., Fournier, T., & Renaud, P. (2003). Anxiety and presence during VR immersion: a comparative study of the reactions of phobic and non-phobic participants in therapeutic virtual environments derived from computer games. *Cyberpsychol.Behav., 6,* 467-476.

Rolls, E. T. (2000). The orbitofrontal cortex and reward. *Cereb.Cortex, 10,* 284-294.

Rolls, E. T. (2004). The functions of the orbitofrontal cortex. *Brain Cogn, 55,* 11-29.

Rolls, E. T., Critchley, H. D., Browning, A., & Hernadi, I. (1998). The neurophysiology of taste and olfaction in primates, and umami flavor. *Ann.N.Y.Acad.Sci., 855,* 426-437.

Rotshtein, P., Malach, R., Hadar, U., Graif, M., & Hendler, T. (2001). Feeling or features: different sensitivity to emotion in high-order visual cortex and amygdala. *Neuron, 32,* 747-757.

Rowe, J. B., Toni, I., Josephs, O., Frackowiak, R. S., & Passingham, R. E. (2000). The prefrontal cortex: response selection or maintenance within working memory? *Science, 288,* 1656-1660.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S. C., Simmons, A. et al. (2000). Functional frontalisation with age: mapping neurodevelopmental trajectories with fMRI. *Neurosci.Biobehav.Rev., 24,* 13-19.

Rubia, K., Smith, A. B., Brammer, M. J., & Taylor, E. (2003). Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. *Neuroimage., 20,* 351-358.

Sadato, N., Nakamura, S., Oohashi, T., Nishina, E., Fuwamoto, Y., Waki, A. et al. (1998). Neural networks for generation and suppression of alpha rhythm: a PET study. *Neuroreport, 9,* 893-897.

Samson, S. & Zatorre, R. J. (1992). Learning and retention of melodic and verbal information after unilateral temporal lobectomy. *Neuropsychologia, 30,* 815-826.

Sander, K., Brechmann, A., & Scheich, H. (2003). Audition of laughing and crying leads to right amygdala activation in a low-noise fMRI setting. *Brain Res.Brain Res.Protoc., 11,* 81-91.

Sander, K. & Scheich, H. (2001). Auditory perception of laughing and crying activates human amygdala regardless of attentional state. *Brain Res.Cogn Brain Res., 12,* 181-198.

Santhouse, A. M., Howard, R. J., & ffytche, D. H. (2000). Visual hallucinatory syndromes and the anatomy of the visual brain. *Brain, 123 (Pt 10),* 2055-2064.

Sato, W., Yoshikawa, S., Kochiyama, T., & Matsumura, M. (2004). The amygdala processes the emotional significance of facial expressions: an fMRI investigation using the interaction between expression and face direction. *Neuroimage., 22,* 1006-1013.

Schachter, S. (1962). Cognitive, social, and physiological determinants of emotional states. *Psychological Review, 69,* 379-399.

Schaik, P., Turnbull, T., Wersch, A., & Drummond, S. (2004). Presence within a mixed reality environment. *Cyberpsychol.Behav., 7,* 540-552.

Schandry, R. (1996). *Lehrbuch Psychophysiologie*. Weinheim: Psychologie Verlags Union.

Schapkin, S. A., Gusev, A. N., & Kuhl, J. (2000). Categorization of unilaterally presented emotional words: an ERP analysis. *Acta Neurobiol.Exp.(Wars.), 60,* 17-28.

Scherer, K. R. (2000). Psychological models of emotion. In J.C.Borod (Ed.), *The Neuropsychology of Emotion* (pp. 137-162). New York: Oxford University Press.

Scherg, M. & Von Cramon, D. (1985). Two bilateral sources of the late AEP as identified by a spatio-temporal dipole model. *Electroencephalography and Clinical Neurophysiology, 62,* 32-44.

Schmidt, L. A. & Trainor, L. J. (2001). Frontal brain electrical activity (EEG) distinguishes valence and intensity of musical emotions. *Cognition and Emotion, 15,* 487-500.

Schneider, F., Gur, R. C., Gur, R. E., & Muenz, L. R. (1994). Standardized mood induction with happy and sad facial expressions. *Psychiatry Res., 51,* 19-31.

Schubert, T. (2002). Five theses on the book problem: Presence in books, film and VR. 5th Annual International Workshop on Presence 9-11 October 2002 Porto, Portugal. Ref Type: Hearing

Schubert, T., Friedmann, F., & Regenbrecht, H. (1999). Embodied Presence in Virtual Environments. In R.Paton & I. Neilson (Eds.), *Visual Representations and Interpretations* (pp. 268-278). London: Springer-Verlag.

Schubert, T., Friedmann, F., & Regenbrecht, H. (2001). The experience of Presence: Factor analytic insights. *Presence: Teleoperators And Virtual Environments, 10,* 266-281.

Segalowitz, S. J. & Davies, P. L. (2004). Charting the maturation of the frontal lobe: an electrophysiological strategy. *Brain Cogn, 55,* 116-133.

Sergent, J., Ohta, S., & MacDonald, B. (1992). Functional neuroanatomy of face and object processing. A positron emission tomography study. *Brain, 115 Pt 1,* 15-36.

Sheridan, T. B. (1992). Musings on telepresence and virtual presence. *Presence: Teleoperators And Virtual Environments, 1,* 120-125.

Shin, L. M., Dougherty, D. D., Orr, S. P., Pitman, R. K., Lasko, M., Macklin, M. L. et al. (2000). Activation of anterior paralimbic structures during guilt-related script-driven imagery. *Biol.Psychiatry, 48,* 43-50.

Sholl, M. J. (1999). Egocentric frames of reference used for the retrieval of survey knowledge learned by map and navigation. *Spatial Cognition and Computation, 1,* 475-494.

Silva, L. R., Amitai, Y., & Connors, B. W. (1991). Intrinsic oscillations of neocortex generated by layer 5 pyramidal neurons. *Science, 251,* 432-435.

Simpson, J. R., Ongur, D., Akbudak, E., Conturo, T. E., Ollinger, J. M., Snyder, A. Z. et al. (2000). The emotional modulation of cognitive processing: an fMRI study. *J.Cogn Neurosci., 12 Suppl 2,* 157-170.

Skaggs, W. E., McNaughton, B. L., Wilson, M. A., & Barnes, C. A. (1996). Theta phase precession in hippocampal neuronal populations and the compression of temporal sequences. *Hippocampus, 6,* 149-172.

Slater, M. (2002). Presence and the Sixth Sense. *Presence: Teleoperators And Virtual Environments, 11,* 435-439.

Slater, M., Steed, A., McCarthy, J., & Maringelli, F. (1998). The influence of body movement on subjective presence in virtual environments. *Hum.Factors, 40,* 469-477.

Slater, M., Usoh, M., & Steed, A. (1995). Taking Steps: The influence of a Walking Metaphor on Presence in Virtual Reality. *ACM Transactions on Computer Human Interaction, 2,* 201-219.

Small, D. M., Gregory, M. D., Mak, Y. E., Gitelman, D., Mesulam, M. M., & Parrish, T. (2003). Dissociation of neural representation of intensity and affective valuation in human gustation. *Neuron, 39,* 701-711.

Small, D. M., Zatorre, R. J., Dagher, A., Evans, A. C., & Jones-Gotman, M. (2001). Changes in brain activity related to eating chocolate: from pleasure to aversion. *Brain, 124,* 1720-1733.

Smith, E. E. & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283,* 1657-1661.

Smith, S. D. & Bulman-Fleming, M. B. (2005). An examination of the right-hemisphere hypothesis of the lateralization of emotion. *Brain Cogn, 57,* 210-213.

Sowell, E. R., Thompson, P. M., Holmes, C. J., Batth, R., Jernigan, T. L., & Toga, A. W. (1999). Localizing age-related changes in brain structure between childhood and adolescence using statistical parametric mapping. *Neuroimage., 9,* 587-597.

Sowell, E. R., Thompson, P. M., Tessner, K. D., & Toga, A. W. (2001). Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: Inverse relationships during postadolescent brain maturation. *J.Neurosci., 21,* 8819-8829.

Stark, R., Schienle, A., Walter, B., Kirsch, P., Blecker, C., Ott, U. et al. (2004). Hemodynamic effects of negative emotional pictures - a test-retest analysis. *Neuropsychobiology, 50,* 108-118.

Stemmler, G., Heldmann, M., Pauls, C. A., & Scherer, T. (2001). Constraints for emotion specificity in fear and anger: the context counts. *Psychophysiology, 38,* 275-291.

Steuer, J. (1995). Defining virtual reality: Dimensions determining telepresence. In F.Biocca & M. R. Levy (Eds.), *Communication in the age of virtual reality* (pp. 33-56). Hillsdale,NJ: Lawrence Erlbaum Associates.

Stoleru, S., Gregoire, M. C., Gerard, D., Decety, J., Lafarge, E., Cinotti, L. et al. (1999). Neuroanatomical correlates of visually evoked sexual arousal in human males. *Arch.Sex Behav., 28,* 1-21.

Surguladze, S. A., Brammer, M. J., Young, A. W., Andrew, C., Travis, M. J., Williams, S. C. et al. (2003). A preferential increase in the extrastriate response to signals of danger. *Neuroimage., 19,* 1317-1328.

Talairach, J. & Tournoux, P. (1988). *Co-Planar Stereotaxic Atlas of the Human Brain*. Stuttgart: Thieme.

Tamm, L., Menon, V., & Reiss, A. L. (2002). Maturation of brain function associated with response inhibition. *J.Am.Acad.Child Adolesc.Psychiatry, 41,* 1231-1238.

Tataranni, P. A., Gautier, J. F., Chen, K., Uecker, A., Bandy, D., Salbe, A. D. et al. (1999). Neuroanatomical correlates of hunger and satiation in humans using positron emission tomography. *Proc.Natl.Acad.Sci.U.S.A, 96,* 4569-4574.

Taylor, G. J., Ryan, D. P., & Bagby, R. M. (1985). Toward the development of a new self-report alexithymia scale. *Psychotherapy and Psychosomatics, 44,* 191-199.

Taylor, S. F., Kornblum, S., Lauber, E. J., Minoshima, S., & Koeppe, R. A. (1997). Isolation of specific interference processing in the Stroop task: PET activation studies. *Neuroimage., 6,* 81-92.

Taylor, S. F., Liberzon, I., Fig, L. M., Decker, L. R., Minoshima, S., & Koeppe, R. A. (1998). The effect of emotional content on visual recognition memory: a PET activation study. *Neuroimage., 8,* 188-197.

Taylor, S. F., Liberzon, I., & Koeppe, R. A. (2000). The effect of graded aversive stimuli on limbic and visual activation. *Neuropsychologia, 38,* 1415-1425.

Taylor, S. F., Phan, K. L., Decker, L. R., & Liberzon, I. (2003). Subjective rating of emotionally salient stimuli modulates neural activity. *Neuroimage., 18,* 650-659.

Teasdale, J. D., Howard, R. J., Cox, S. G., Ha, Y., Brammer, M. J., Williams, S. C. et al. (1999). Functional MRI study of the cognitive generation of affect. *Am.J.Psychiatry, 156,* 209-215.

Terwogt, M. M. & van Grinsven, F. (1988). Recognition of emotions in music by children and adults. *Perceptual and Motor Skills, 67,* 697-698.

Terwogt, M. M. & van Grinsven, F. (1991). Musical expression of moodstates. *Psychology of Music, 19,* 99-109.

Thayer, J. F. & Levenson, R. W. (1983). Effects of music on psychophysiological responses to a stressful film. *Psychomusicology, 3,* 44-52.

Toni, I., Schluter, N. D., Josephs, O., Friston, K., & Passingham, R. E. (1999). Signal-, set- and movement-related activity in the human brain: an event-related fMRI study. *Cereb.Cortex, 9,* 35-49.

Towle, V. L., Bolanos, J., Suarez, D., Tan, K., Grzeszczuk, R., Levin, D. N. et al. (1993). The spatial location of EEG electrodes: locating the best-fitting sphere relative to cortical anatomy. *Electroencephalogr.Clin.Neurophysiol., 86,* 1-6.

Trainor, L. J., Desjardins, R. N., & Rockel, C. (1999). A comparison of contour and interval processing in musicians and nonmusicians using event-related potentials. *Australian Journal of Psychology, 51,* 147-153.

Tremblay, L. & Schultz, W. (1999). Relative reward preference in primate orbitofrontal cortex. *Nature, 398,* 704-708.

Tsang, C. D., Trainor, L. J., Santesso, D. L., Tasker, S. L., & Schmidt, L. A. (2001). Frontal EEG responses as a function of affective musical features. *Ann.N.Y.Acad.Sci., 930,* 439-442.

Turner, R., Howseman, A., Rees, G., & Josephs, O. (1997). Functional imaging with magnetic resonance. In R.S.J.Franckowiak, K. J. Friston, C. D. Frith, R. J. Dolan, & J. C. Mazziotta (Eds.), *Human brain function* (pp. 467-486). San Diego: Academic Press.

Tzourio, N., Crivello, F., Mellet, E., Nkanga-Ngila, B., & Mazoyer, B. (1998). Functional anatomy of dominance for speech comprehension in left handers vs right handers. *Neuroimage., 8,* 1-16.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N. et al. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage., 15,* 273-289.

Uchiyama, Y., Ebe, K., Kozato, A., Okada, T., & Sadato, N. (2003). The neural substrates of driving at a safe distance: a functional MRI study. *Neurosci.Lett., 352,* 199-202.

Vastfjall, D. (2003). The subjective sense of presence, emotion recognition, and experienced emotions in auditory virtual environments. *Cyberpsychol.Behav., 6,* 181-188.

Von Holst, E. & Mittelstaedt, H. (1950). Das Reafferenzprinzip. *Naturwissenschaften, 37,* 464-476.

Vorderer, P., Wirth, W., Saari, T., Baumgartner, T., Jancke, L., & et al. (2004). MEC Spatial Presence Questionnaire (MEC SPQ): Short Documentation and Instructions for Application.
Ref Type: Unpublished Work

Walker, A. & Grolnick, W. (1983). *Inf.Behav.Dev., 6,* 491-498.

Walter, H., Vetter, S. C., Grothe, J., Wunderlich, A. P., Hahn, S., & Spitzer, M. (2001). The neural correlates of driving. *Neuroreport, 12,* 1763-1767.

Wedin, L. A. (1972). A multidimentional study of perceptual-emotional qualities in music. *Scandinavian Journal of Psychology, 13,* 241-257.

Westwood, J. D., Hoffman, H. M., Robb, R. A., & Stredney, D. (1999). *Medicine meets virtual reality: The convergence of physical and informational technologies options for a new era in healthcare*. Amsterdam: IOS Press.

Wiederhold, B. K., Davis, R., & Wiederhold, M. D. (1998). The effects of immersiveness on physiology. In G.Riva, B. K. Wiederhold, & E. Molinari (Eds.), *Virtual environments in clinical psychology and neuroscience* (Amsterdam: Ios Press.

Wiederhold, B. K., Jang, D. P., Gevirtz, R. G., Kim, S. I., Kim, I. Y., & Wiederhold, M. D. (2002a). The treatment of fear of flying: a controlled study of imaginal and virtual reality graded exposure therapy. *IEEE Trans.Inf.Technol.Biomed., 6,* 218-223.

Wiederhold, B. K., Jang, D. P., Kim, S. I., & Wiederhold, M. D. (2002b). Physiological monitoring as an objective tool in virtual reality therapy. *Cyberpsychology & Behavior, 5,* 77-82.

Wild, T. C., Kuiken, D., & Schopflocher, D. (1995). The role of absorption in experiental involvement. *Journal of Personality and Social Psychology, 69,* 569-579.

Wilkins, A. J., Shallice, T., & McCarthy, R. (1987). Frontal lesions and sustained attention. *Neuropsychologia, 25,* 359-365.

Williams, B. R., Ponesse, J. S., Schachar, R. J., Logan, G. D., & Tannock, R. (1999). Development of inhibitory control across the life span. *Dev.Psychol., 35,* 205-213.

Wirth, W., Hartmann, T., Böcking, S., Vorderer, P., Klimmt, C., Schramm, H. et al. (2005). A Two-Level Model of the Formation of Spatial Presence Experience. *Communication Yearbook, submitted for publication*.

Worsley, K. J., Andermann, M., Koulis, T., MacDonald, D., & Evans, A. C. (1999). Detecting changes in nonisotropic images. *Hum.Brain Mapp., 8,* 98-101.

Worsley, K. J., Liao, C. H., Aston, J., Petre, V., Duncan, G. H., Morales, F. et al. (2002). A general statistical analysis for fMRI data. *Neuroimage., 15,* 1-15.

Wundt (1905). *Grundriss der Psychologie*. Leipzig: Engelman.

Yeomans, J. S. & Frankland, P. W. (1995). The acoustic startle reflex: neurons and connections. *Brain Research Reviews, 21,* 301-314.

Zahorik, P. & Jenison, R. L. (1998). Presence as Being-in-the-World. *Presence: Teleoperators And Virtual Environments, 7,* 78-89.

Zatorre, R. J., Belin, P., & Penhune, V. B. (2002). Structure and function of auditory cortex: music and speech. *Trends Cogn Sci., 6,* 37-46.

Zatorre, R. J., Evans, A. C., & Meyer, E. (1994). Neural mechanisms underlying melodic perception and memory for pitch. *J.Neurosci., 14,* 1908-1919.

Zeki, S. & ffytche, D. H. (1998). The Riddoch syndrome: insights into the neurobiology of conscious vision. *Brain, 121 (Pt 1),* 25-45.

Zillman, D. (1978). Attribution and misattribution of excitatory reactions. In R.J.Harvey, W. I. Ickes, & R. F. Kidd (Eds.), *New directions in attribution research* (Hillsdale, NJ: Erlbaum.

Zung, W. W. K. (1965). A Self-Rating Depression Scale. *Archives of General Psychiatry, 12,* 63-70.

10 Tables: Study A, B and C

Table 10.1: Mean psychometrical ratings (± standard deviation) of the fear, happy and sad conditions (combined, picture, sound) regarding 4 scales (happiness, sadness, fear and involvement 5-point scales, ranking from "1 = not at all" to "5 = very strongly")

	Fear condition			**Happy condition**			**Sad condition**		
	Combined	Picture	Sound	Combined	Picture	Sound	Combined	Picture	Sound
Happiness scale	1,06 (±0.20)	1,04 (±0.15)	2,08 (±1.10)	4,44 (±0.58)	4,12 (±0.71)	4,33 (±0.59)	1,08 (±0.23)	1,11 (±0.23)	1,86 (±0.99)
Sadness Scale	3,16 (±0.87)	3,44 (±0.90)	2,02 (±0.81)	1,01 (±0.68)	1,11 (±0.23)	1,12 (±0.26)	4,15 (±0.56)	3,75 (±0.84)	3,29 (±1.22)
Fear scale	3,81 (±0.67)	3,7 (±0.97)	2,94 (±1.23)	1,01 (±0.68)	1,02 (±0.14)	1,02 (±0.09)	2,27 (±0.86)	2,02 (±0.95)	1,83 (±0.69)
Involvement scale	4,19 (±0.67)	3,84 (±0.91)	3,94 (±0.63)	4,26 (±0.54)	3,61 (±0.98)	4,13 (±0.68)	4,48 (±0.69)	3,7 (±0.78)	4,19 (±0.72)

Table 10.2: Peak activations observed for the contrast combined versus fixation (C>F).

Brain regions	BA	Side	x	y	z	Max t Score	Voxels
Frontal Lobe							
Precentral Gyrus	6	R	48	0	40	8.16 **	14
Temporal Lobe							
Superior Temporal Gyrus	22/38	L	-44	12	-28	6.71 **	22
	22	R	52	-20	-4	5.60 *	60
Middle Temporal Gyrus	21/38	R	56	-4	-20	6.26 *	22
	21/38	L	-32	4	-40	6.57 **	44
Inferior Temporal Gyrus	20	L	-40	-8	-36	5.11 *	38
Parahippocampus / Uncus	35/36	L	-20	-4	-28	14.16 ***	59
	35/36	R	20	-24	-24	6.73 **	64
Hippocampus		L	-24	-8	-24	8.58 **	36
Hippocampus		R	32	-28	-12	5.19 *	21
Amygdala		L	-20	-4	-24	8.08 **	9
Occipital Lobe							
Middle occipital gyrus	18/19	L	-28	-96	8	6.11 *	128
		R	28	-92	16	6.74 **	83
Inferior occipital gyrus	17/18/19	L/R	12	-92	-16	8.42 **	113
Cuneus	18	L	-16	-100	0	7.30 **	
Fusiform Gyrus	18/19/20	L	-24	-88	-24	12.18 ***	31
	18/19/20	R	24	-87	-24	8.21 **	43
Subcortical Structures							
Cerebellum		L	-4	-36	-8	11.61 ***	105
		R	40	-56	-36	7.83 **	233
Pons		R	8	-32	-32	4.70 *	15

The coordinates are given according to the MNI space together with its T-scores and significant thresholds (*P < 0.001, ** P < 0.0001 ***P < 0.00001 (all uncorrected for multiple comparisons). Minimum cluster size 5 voxels. For every structure only the highest maxima for the left and right hemisphere are reported.

Table 10.3: Peak activations observed for the contrast picture versus fixation (P>F).

Brain regions	BA	Side	x	y	z	Max t Score	Voxels
Frontal Lobe							
Inferior Frontal Gyrus	44/45	R	52	8	32	7.11 **	56
Middle Frontal Gyrus	45	L	-52	32	20	4.38 *	6
Temporal Lobe							
Parahippocampus/Hippocampus	27	L	-20	-32	-8	4.89 *	12
	28	R	20	-28	-12	5.42 *	9
Occipital Lobe							
Middle occipital gyrus	18/19	L	-40	-80	0	11.90 ***	130
	18/19	R	28	-92	16	12.05 ***	65
Inferior occipital gyrus	17/18/19	L	-12	-96	-16	7.59 **	134
	17/18/19	R	12	-96	-16	9.03 ***	140
Cuneus	18	L	-20	-100	0	11.34 ***	18
Fusiform Gyrus	18/19	L	-24	-88	-24	10.55 ***	23
	18/19	R	22	-86	-20	4.82 *	33
Subcortical Structures							
Cerebellum		L	-48	-64	-28	6.29 *	175
		R	24	-88	-28	9.12 ***	202

The coordinates are given according to the MNI space together with its T-scores and significant thresholds (*P < 0.001, ** P < 0.0001, ***P < 0.00001 (all uncorrected for multiple comparisons). Minimum cluster size 5 voxels. For every structure only the highest maxima for the left and the right hemisphere are reported.

Table 10.4: Peak activations observed for the contrasts picture versus combined (P>C) and combined versus picture (C>P). Note that all emotional conditions were only composed of negative stimuli (fear and sad, see methods part for an explanation).

	Brain regions	BA	Side	x	y	z	Max t Score	Voxels
Picture versus Combined (P>C)	**Frontal Lobe**							
	Inferior Frontal Gyrus	44	R	52	24	28	5.37 **	50
	Middle Frontal Gyrus	45/46	R	48	44	8	4.88 *	17
	Superior Frontal Gyrus	8	L	-4	28	52	4.03 *	8
Combined versus Picture (C>P)	**Frontal Lobe**							
	Medial Frontal Gyrus	11	L/R	0	44	-16	3.98 *	15
	Precentral Gyrus	6	R	52	0	44	6.05 **	8
	Temporal Lobe							
	Superior Temporal Gyrus	21	R	56	-20	-4	8.54 ***	235
		22	R	60	-24	4	8.00 ***	
		38	R	36	12	-32	4.36 *	
		41	R	56	-28	8	7.82 ***	
		42	L	-64	-28	8	8.43 ***	162
		22	L	-56	-16	0	6.57 **	
	Middle Temporal Gyrus	21	R	56	0	-20	10.34 ***	156
		21	R	64	-16	-12	7.65 ***	
		38	R	40	12	-44	5.52 **	
		21	L	-52	8	-28	6.70 **	142
	Parahippocampus	28	R	16	-8	-32	7.81 ***	27
		28	R	24	-16	-20	4.68 *	
		36	L	-26	-20	-28	5.10 **	36
	Amygdala		L	-17	-4	-20	5.89 **	7
	Hippocampus/Amygdala		R	24	-8	-24	6.60 **	27
	Hippocampus		L	-24	-20	-16	6.17 **	18
	Fusiform Gyrus	20	L	-32	-20	-32	9.39 ***	38
		20	L	-40	-8	-32	6.48 **	
		20	R	35	-2	-36	4.04 *	17
	Insula	13	L	-36	-8	12	3.68 *	14
	Parietal Lobe							
	Posterior Cingulate / Precuneus	29	L/R	8	-44	16	4.62 *	19
	Subcortical structures							
	Nucleus caudatus		L	-8	16	0	5.95 **	19
			L	-16	4	24	8.51 ***	
	Pons		L/R	4	-24	-36	4.67 *	12
	Cerebellum		L/R	8	-40	-12	4.33 *	17

The coordinates are given according to the MNI space together with its T-scores and significant thresholds (*P < 0.005, ** P < 0.0005, ***P < 0.00005 (all uncorrected for multiple comparisons). Minimum cluster size 5 voxels. All observed maxima are reported.

Table 10.5: Mean ERD/ERS values (± standard error) for children and adolescents broken down for all 3 roller coaster conditions (UP, DOWN, END) and two scalp regions (frontal, parietal).

		Children		Adolescents	
CONDITION	REGION	Mean	SE	Mean	SE
UP	Frontal	3.21	2.92	8.24	2.95
	Parietal	9.21	3.51	9.91	4.37
DOWN	Frontal	-2.25	2.94	5.91	2.76
	Parietal	17.95	3.81	13.31	4.91
END	Frontal	-4.04	2.74	4.54	3.32
	Parietal	7.67	3.95	6.59	4.70

Table 10.6: LORETA results of significant differences in brain electrical activity during the DOWN compared to the CONTROL condition separately for children and adolescents.

	Frequency band			Brain region (Brodmann area)	
Group	Name	Range (Hz)		Left	Right
Children	Theta [d]	4-7	↓ [a]		Inferior parietal lobe (7) (39, -67, 43) [b]
			↓		Superior Parietal gyrus/ Precuneus (7) (4, -60, 43)
			↑	Superior frontal gyrus (6) (-10, -4, 71)	Superior frontal gyrus (6) (11, -4, 71)
			↑	Temporal gyrus (21/20/38) (-59, 3, -6)	
	Alpha [c]	8-12	↓		Precuneus (19,7) (25, -88, 36)
			↓		Posterior Cingulate (29/30) (4, -39, 22)
			↑		Middle frontal gyrus (6/8/9) (32, 10, 57)
			↑		Sub-gyral frontal lobe (6) (25, -4, 57)
			↑	Insula (13) (-38, -18, 15)	Insula (13) (39, -4, 8)
			↑	Postcentral gyrus (3/43) (-66, -11, 22)	Inferior frontal gyrus (9/44/45) (60, 10, 29)
Adolescents	Alpha [c]	8-12	↓	Posterior cingulate (29) (-3, -39, 22)	Posterior cingulate (29) (4, -39, 22))
			↓	Cingulate gyrus (31) (-3, -46, 29)	Cingulate gyrus (31) (4, -46, 29)
			↓	Superior parietal gyrus / Precuneus (7) (-10, -67, 57)	Superior parietal gyrus / Precuneus (7) (11, -63, 57)
	Beta2 [d]	19-21	↑	Precentral gyrus (4) (-59, -4, 22)	
			↑	Inferior frontal gyrus (44/45) (-52, 10, 22)	
			↑	Insula (13) (-38, -11, 1)	

[a] Downward arrows indicate decreases, upward arrows increases of electrical activity for DOWN compared to CONTROL regarding a specific frequency band.
[b] Coordinates are defined in the standard stereotaxic space of Talairach and correspond to the observed activation maxima. Brodmann areas describe the extent of the activated brain region.
[c] $p < 0.05$ (voxel statistic)
[d] $p < 0.10$ (voxel statistic)

11 Figures: Study A, B and C

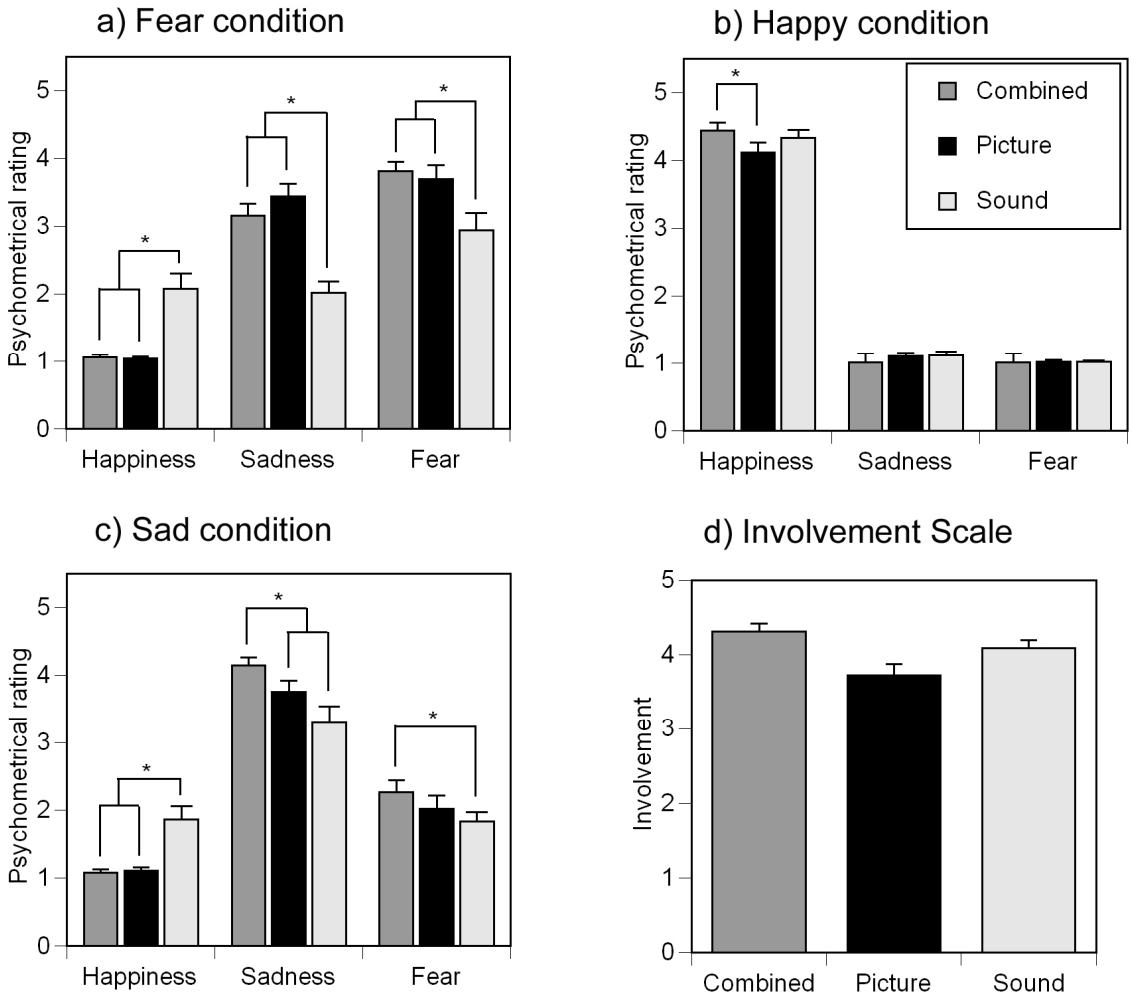

Figure 11.1: Mean psychometrical ratings (± SEM) of the fear conditions (a), happy conditions (b) and sad conditions (c). Note that subjects had to rate every emotion on a scale for happiness, sadness and fear (5-point scales, ranking from "1 = not at all" to "5= very strongly"). Significant statistical differences between the different modalities (combined, picture, sound) are depicted (all at $p < 0.01$). (d) Significant main effect of modality regarding the involvement scale is shown demonstrating an increased involvement experience both in the combined and the sound conditions compared to the picture conditions ($p<0.001$).

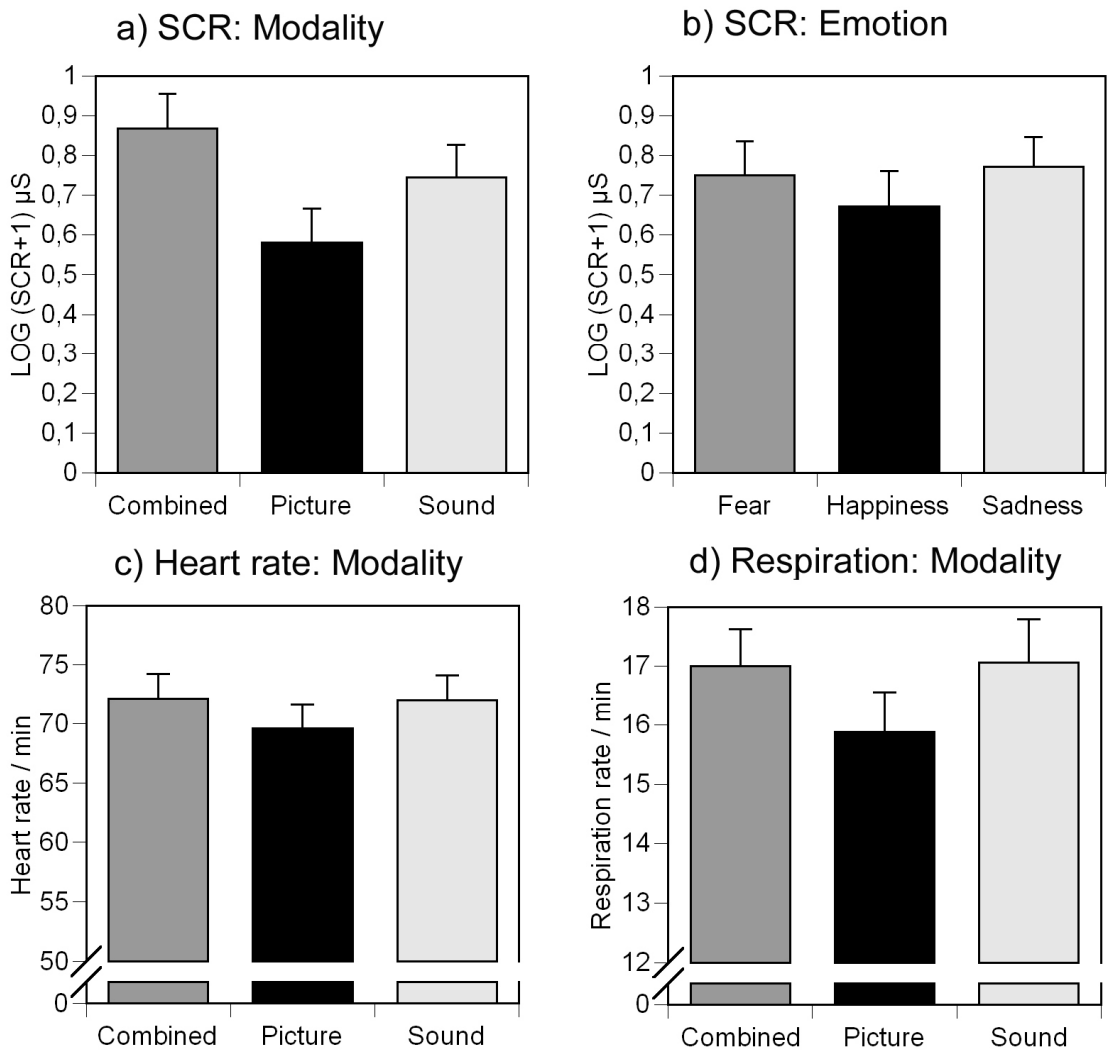

Figure 11.2: Physiological results of SCR (a) and (b), Heart rate (c), and respiration (d). Depicted are means and standard error of the means. (a) Findings demonstrate the largest SCR for the combined conditions, intermediate for the sound conditions and lowest for the picture conditions ($p<0.001$). (b) Negative emotional conditions have larger SCR than the positive emotional conditions ($p<0.05$). (c) and (d) Both heart rate ($p<0.001$) and respiration ($p<0.01$) have increased values in the combined and sound conditions in comparison with the picture conditions.

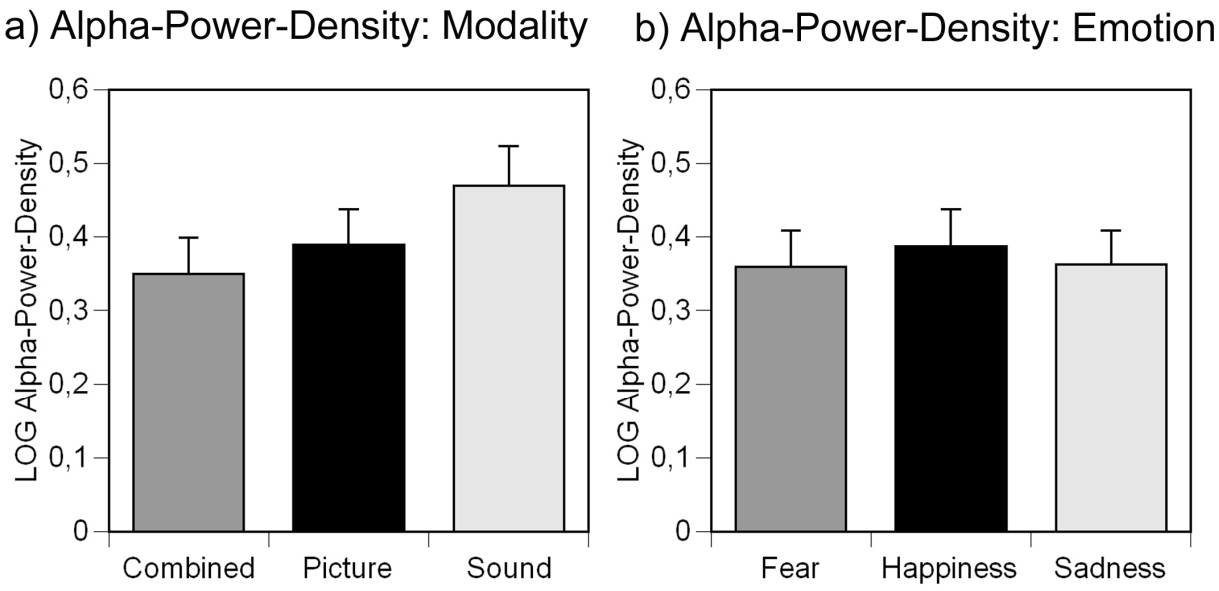

Figure 11.3: Means (± SEM) of log Alpha-Power-Density (8-13 Hz). (a) Depicted is the highly significant main effect of modality ($p<0.001$) indicating the largest Alpha-Power-Activity for the sound conditions, intermediate for the picture conditions and lowest for the combined conditions. (b) Additional four-way repeated-measures ANOVA excluding the sound modality factor (please see text for explanation) revealed a significant main effect of emotion ($p<0.01$) demonstrating increased Alpha-Power-Activity in the happy conditions (combined + picture) compared to the fear and sad conditions.

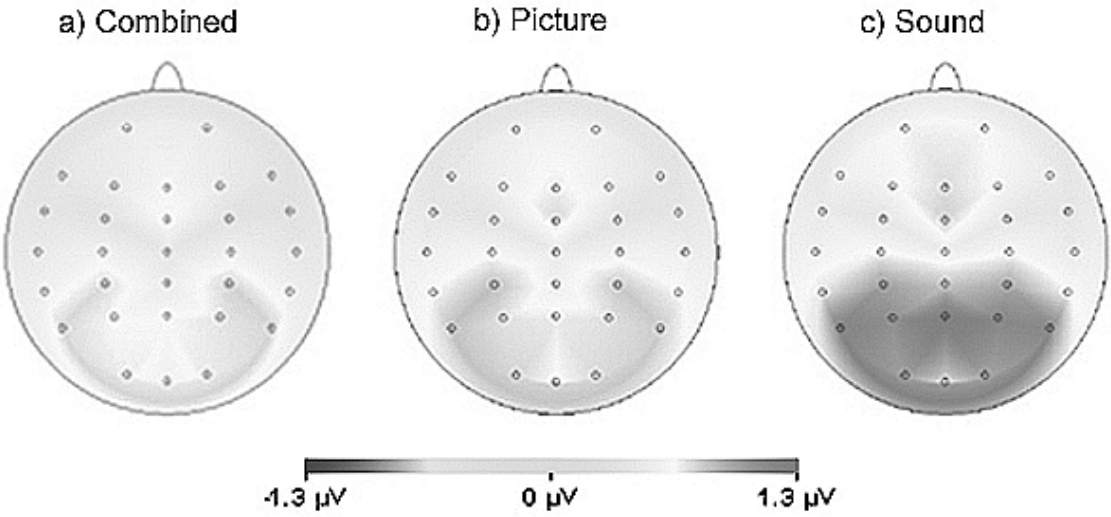

Figure 11.4: Scalp Maps of Alpha-Power-Density (8-13 Hz) in the combined (a), picture (b), and sound conditions (c).

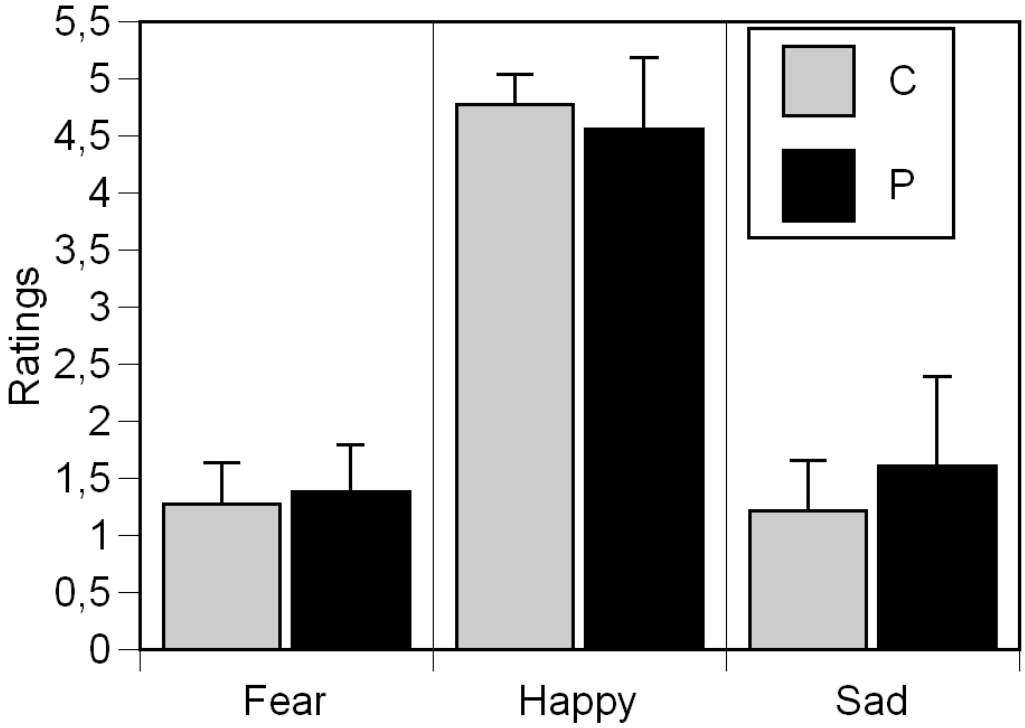

Figure 11.5: Mean valence ratings for all three emotional categories and two modalities (mean ± SD). Depicted is the trend for a significant interaction effect between emotion and modality ($p<0.1$), indicating that the subjects experienced the happy conditions more positive and the fear and sad conditions more negative when congruent emotional music was simultaneously presented. C = Combined, P = Picture.

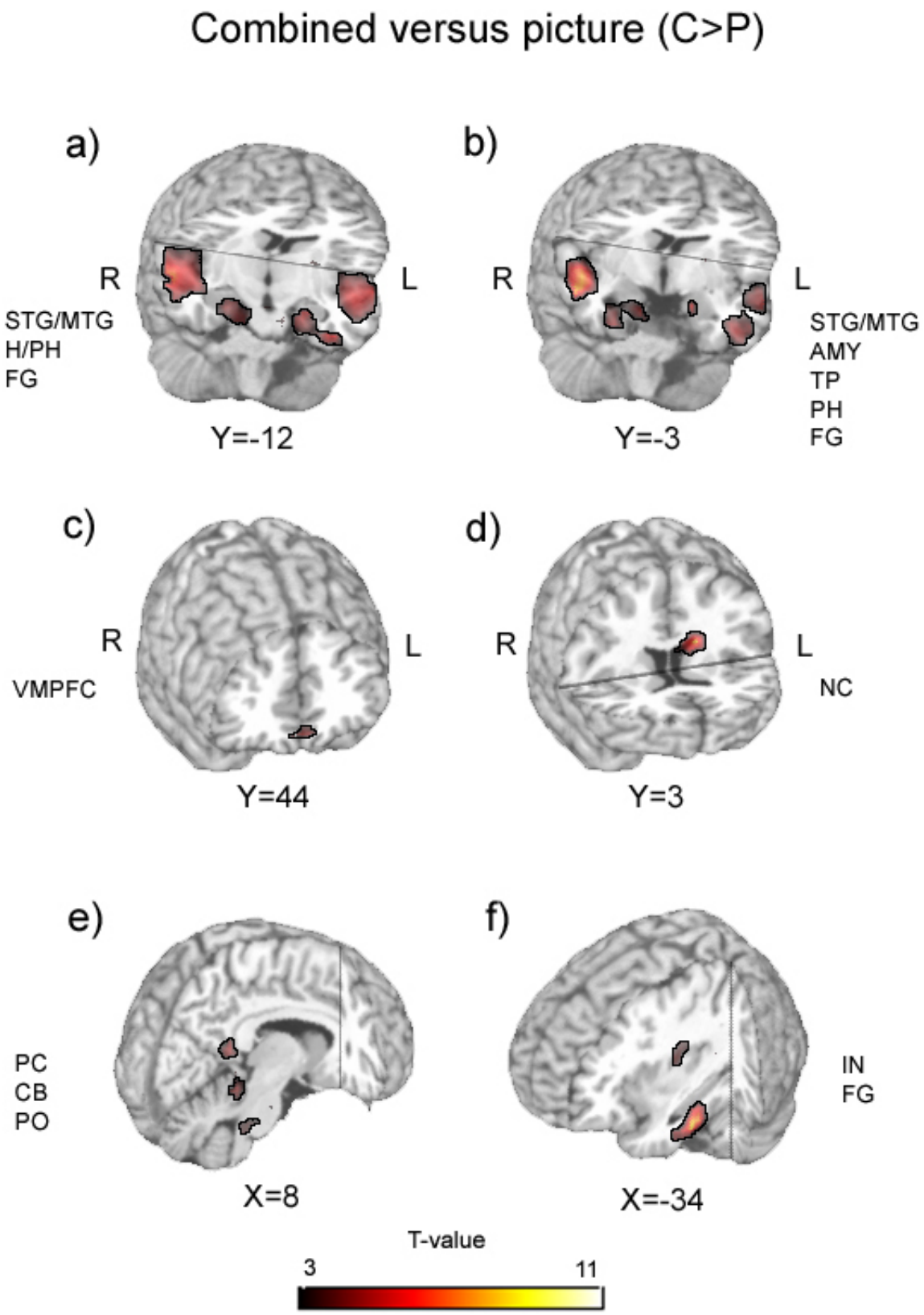

Figure 11.6: Depicted is the increased activity in the combined compared to the picture condition (all $p<0.005$, uncorrected). SPM(t) maps are overlaid on a structural MRI brain. (a) Bilateral superior and middle temporal gyrus (STG, MTG), bilateral hippocampus/parahippocampus (H/PH) and left fusiform gyrus (FG); (b) Bilateral superior and middle temporal gyrus (STG/MTG), left amygdala

(AMY), left temporal pole (TP), right fusiform gyrus/inferior temporal gyrus (FG), right parahippocampus (PH); (c) ventral medial prefrontal cortex (VMPFC); (d) nucleus caudatus (NC); (e) right pons (PO), right cerebellum (CB), right posterior cingulate/precuneus (PC); (f) left fusiform gyrus (FG), left insula (IN).

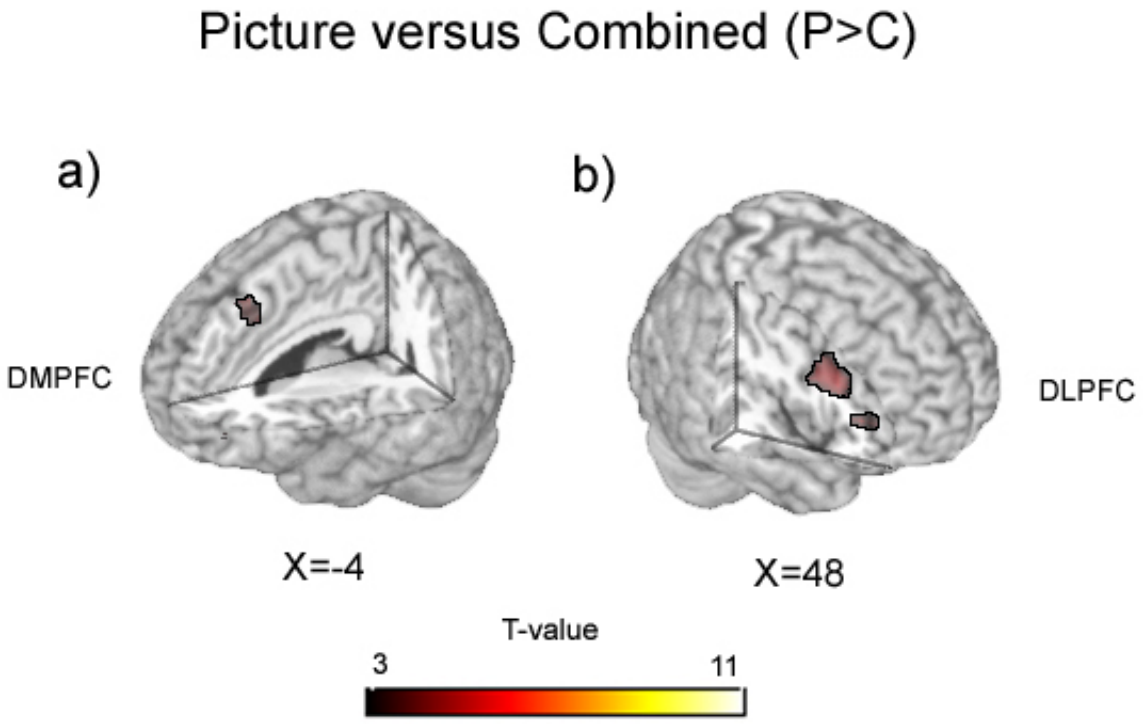

Figure 11.7: Depicted is the increased activity in the picture compared to the combined condition (all $p<0.005$, uncorrected). SPM(t) maps are overlaid on a structural MRI brain. Note that increased activity was only found in the dorsal prefrontal cortex, mainly in the right dorsolateral prefrontal cortex (DLPFC). (a) left dorsomedial prefrontal cortex (DMPFC); (b) right dorsolateral prefrontal cortex (BA 44/45, DLPFC).

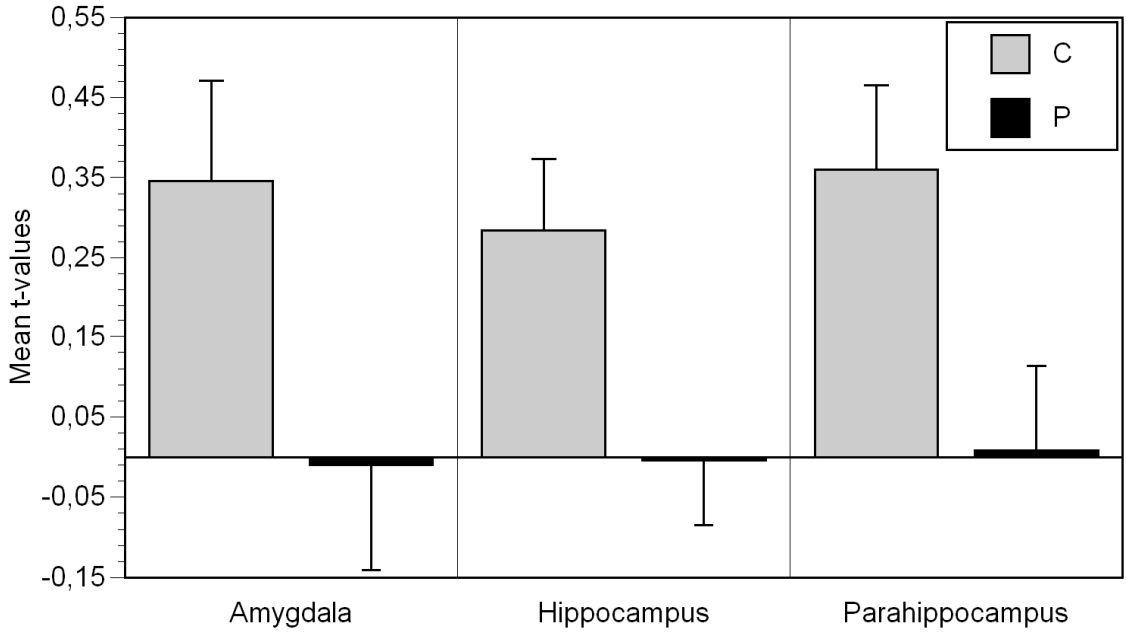

Figure 11.8: Region of interest analysis of the medial temporal lobe system (including amygdala, hippocampus, parahippocampus) using unsmoothed t-values of the contrasts combined versus fixation (C>F) and picture versus fixation (P>F), respectively. Depicted are the significantly increased activations (mean ± SE) in the amygdala, the hippocampus and parahippocampus in the combined (C) relative to the picture (P) condition (main effect of modality, all $p<0.05$). No significant main effect of hemisphere or interaction effect of modality * hemisphere were observed.

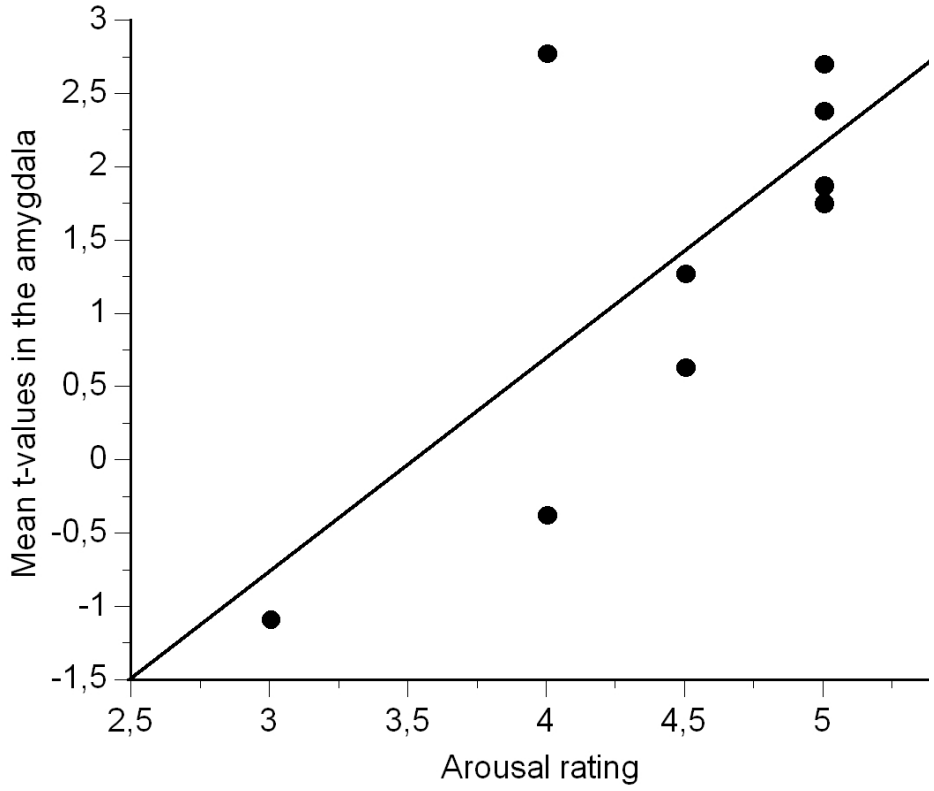

Figure 11.9: Strong positive correlation between the activation of the left and right amygdala in the combined condition and the psychometrical arousal measure obtained at the end of the experiment ($r=0.73$, $p<0.05$). Note that "3" on the rating scale means that the subjects experienced no emotional enhancement in the combined relative to the picture condition, whereas "4" and "5" on this scale means that the subjects experienced the combined condition more arousing than the picture condition.

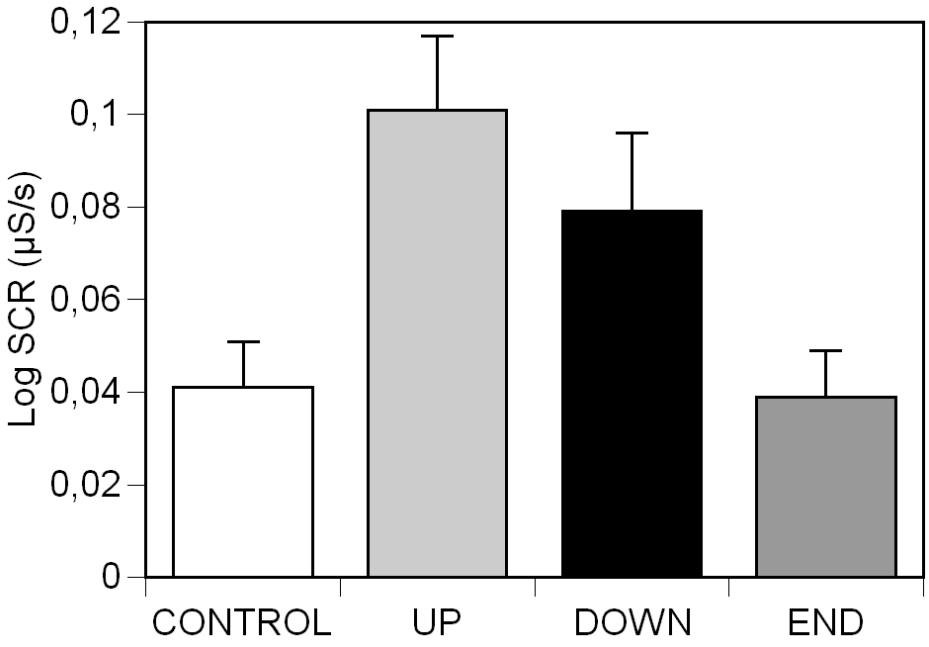

Figure 11.10: Depicted are means (± SE) of the log[SCR+1] in µS per second. Findings demonstrate the largest SCR for UP, intermediate for DOWN and significantly reduced SCR for CONTROL and END. No group differences between children and adolescents were observed.

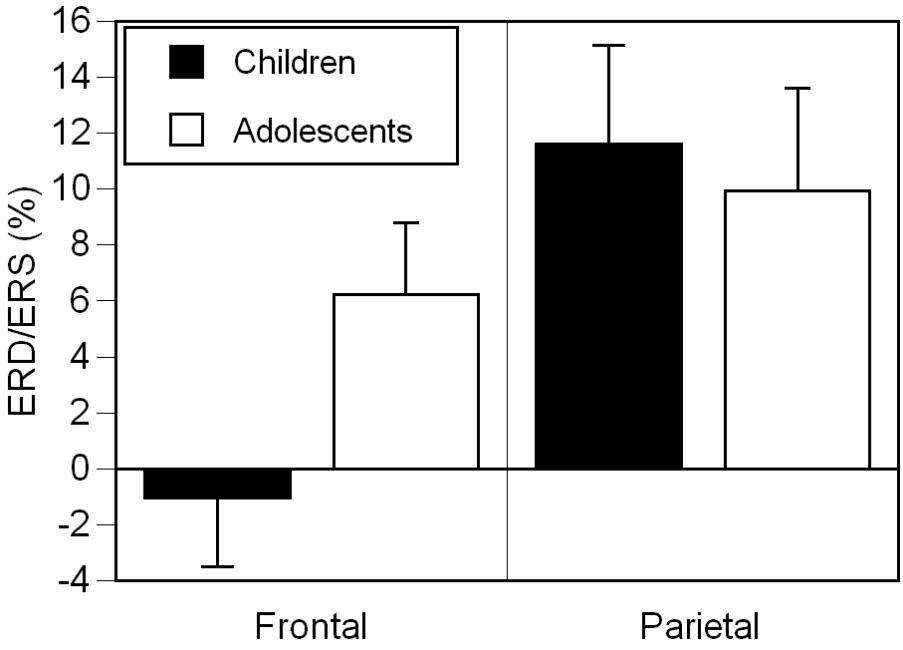

Figure 11.11: Illustrated are means (± SE) of the significant interaction effect of REGION*GROUP (p=0.05) which is qualified by reduced activity at frontal electrodes in children compared to adolescents.

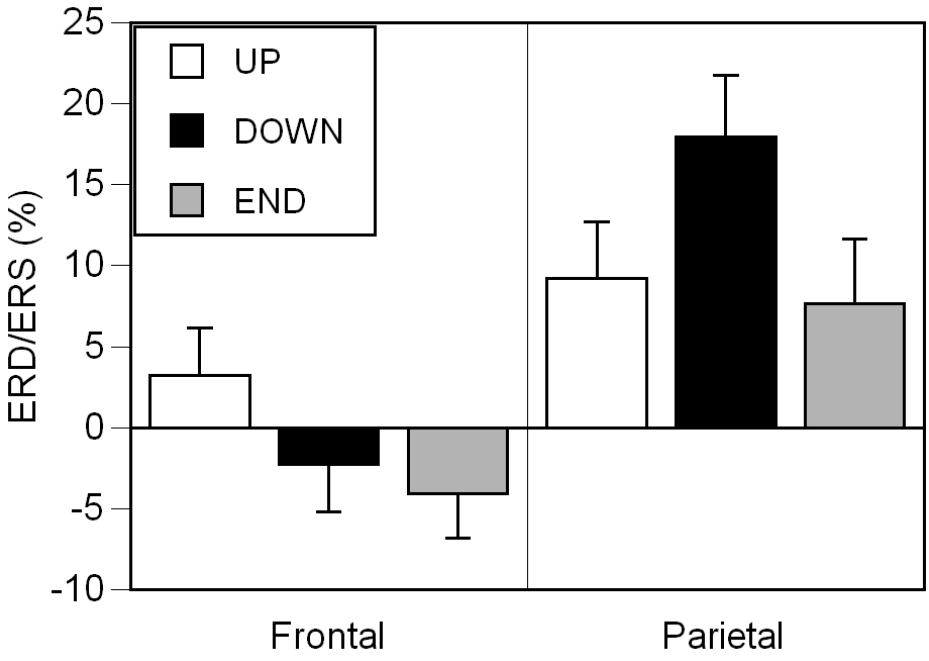

Figure 11.12: Depicted are means (± SE) of the highly significant interaction effect of REGION*COND ($p<0.01$) in children, indicating a clear dissociation between frontal and parietal electrode clusters, which is most pronounced in the DOWN (dynamic roller coaster ride) condition.

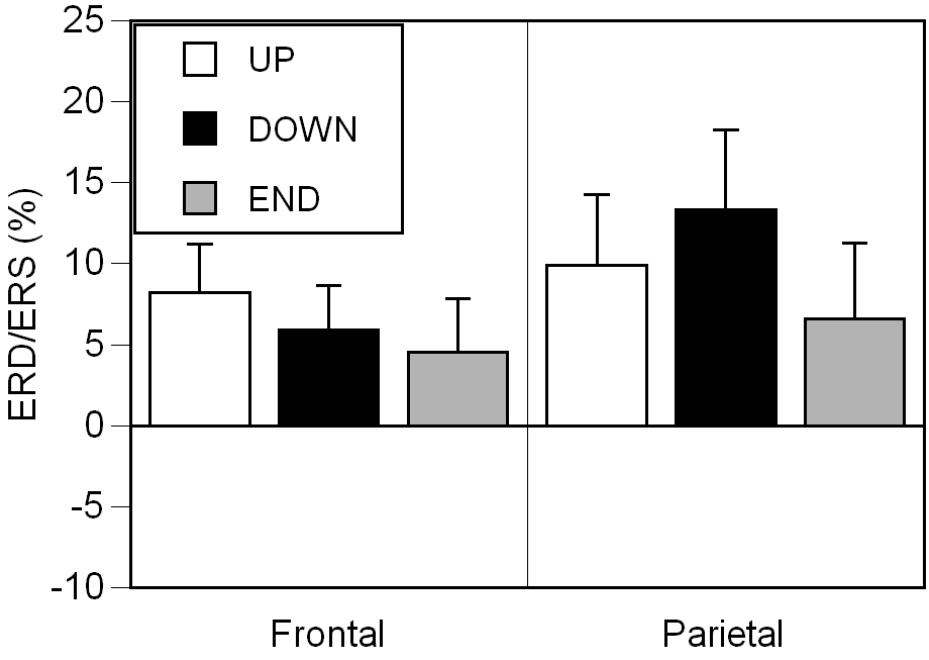

Figure 11.13: Depicted is the significant interaction effect of REGION*COND ($p=0.043$) in adolescents (means ± SE), demonstrating the highest ERD in the DOWN and UP condition. In contrast to children, no ERS (cortical deactivation) could be observed at frontal electrode clusters.

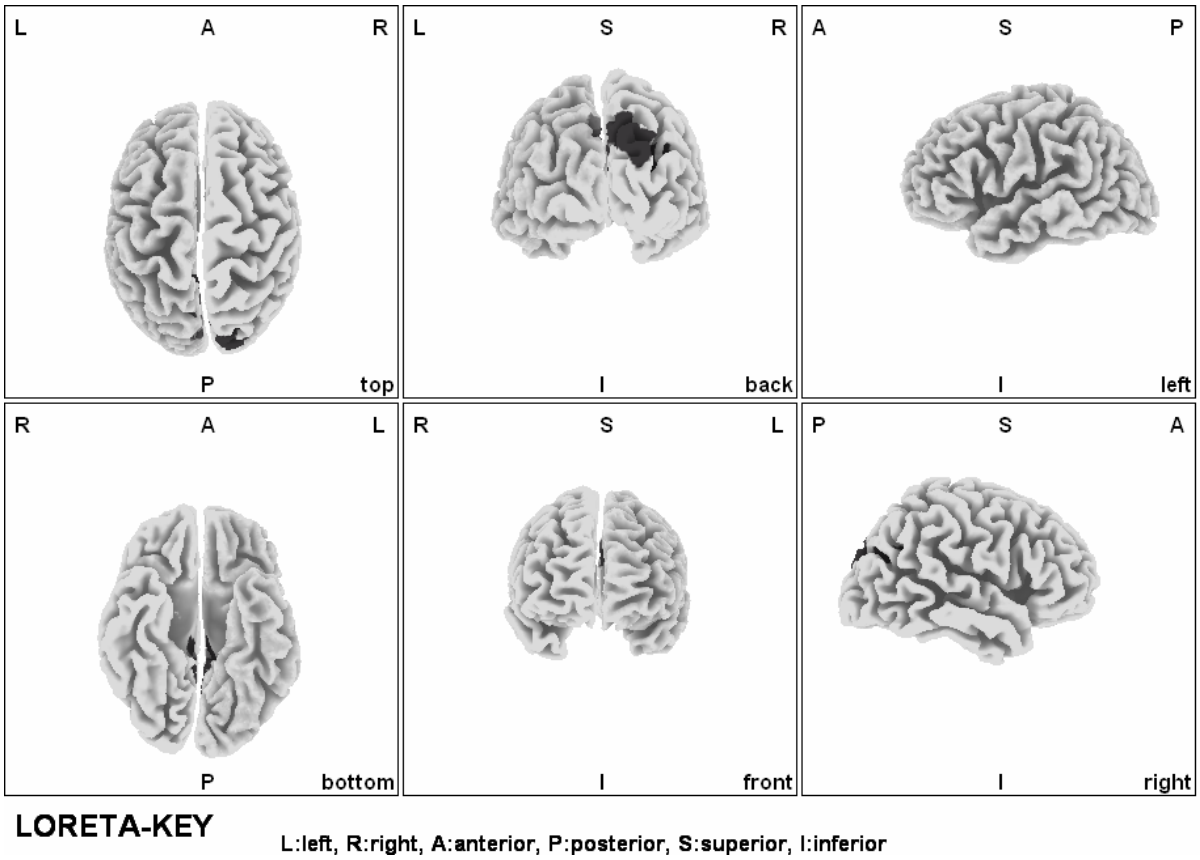

Figure 11.14: LORETA functional images of regional electric activity differences for the comparison "DOWN minus CONTROL" in children. Depicted in black color is the increased Alpha power activity in the CONTROL condition in the right parietal cortex (precuneus, posterior cingulate), indicating increased brain activity in the DOWN condition in the right parietal cortex (note that Alpha power is negatively correlated with activity). Results are displayed on the "fiducial cortical surface" (boundary midway through cortical thickness, Dickson, Drury, & Van Essen, 2001). Cortex is shown in grey scale.

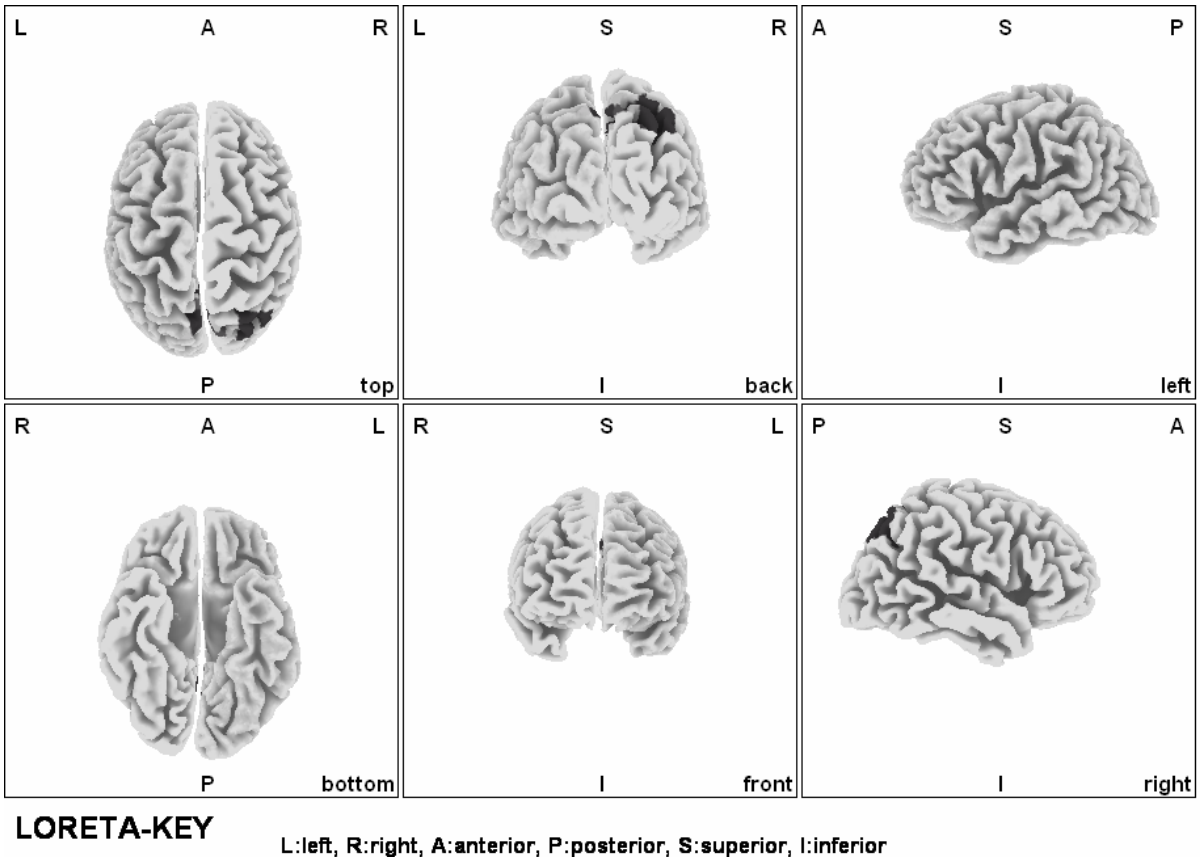

Figure 11.15: LORETA functional images of regional electric activity differences for the comparison "DOWN minus CONTROL" in children. Depicted in black color is the increased Theta power activity in the CONTROL condition in the right parietal cortex (inferior and superior parietal gyrus, precuneus), indicating increased brain activity in the DOWN condition in the right parietal cortex (note that Theta power is negatively correlated with activity). Results are displayed on the "fiducial cortical surface" (boundary midway through cortical thickness, Dickson et al., 2001). Cortex is shown in grey scale.

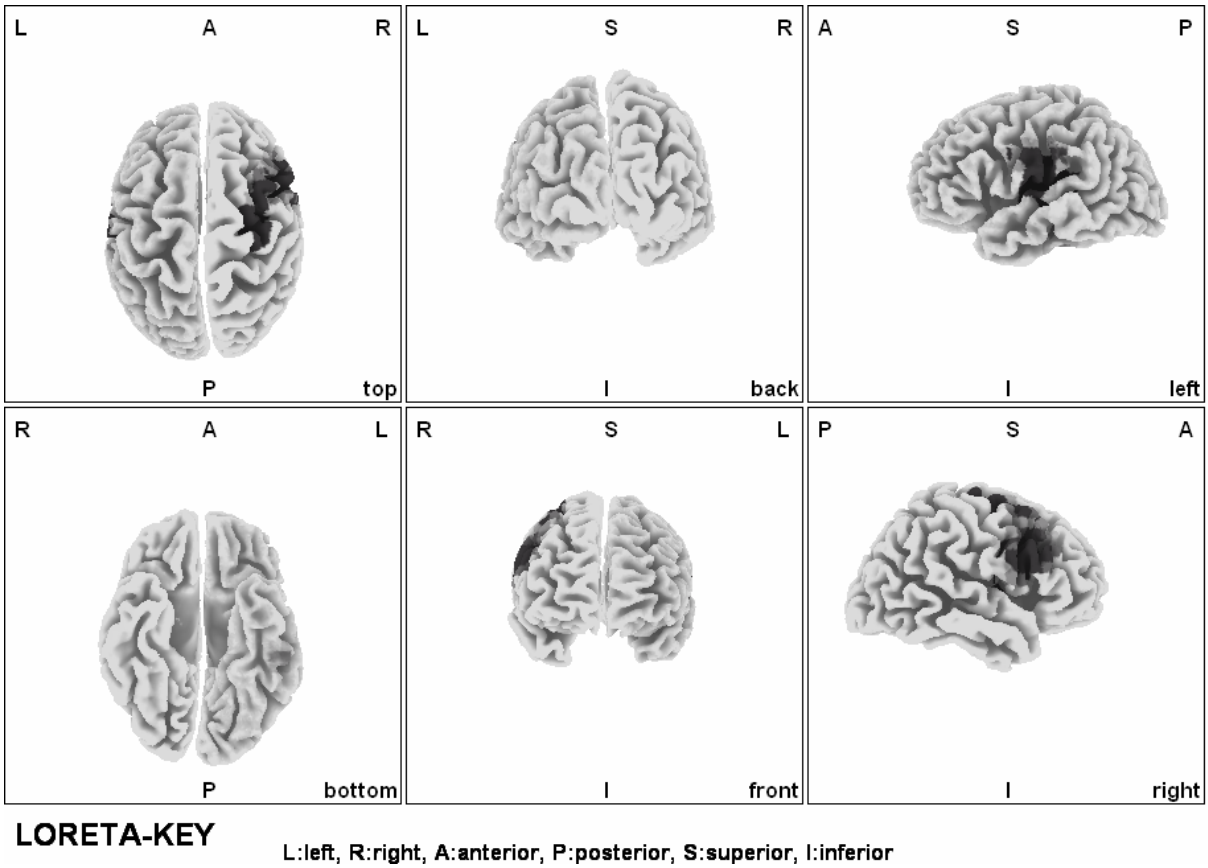

Figure 11.16: LORETA functional images of regional electric activity differences for the comparison "DOWN minus CONTROL" in children. Depicted in black color is the increased Alpha power activity in the DOWN condition in the bilateral insula, left postcentral gyrus, right inferior frontal gyrus and right middle frontal gyrus. Note that increased Alpha power in the inferior and middle frontal gyrus indicates decreased cortical activity in the DOWN condition; whereas the increased Alpha power in the insula and the postcentral gyrus indicates increased cortical activity in the DOWN condition (please see text and chapter 3.2.3.2 for an explanation). Results are displayed on the "fiducial cortical surface" (boundary midway through cortical thickness, Dickson et al., 2001). Cortex is shown in grey scale.

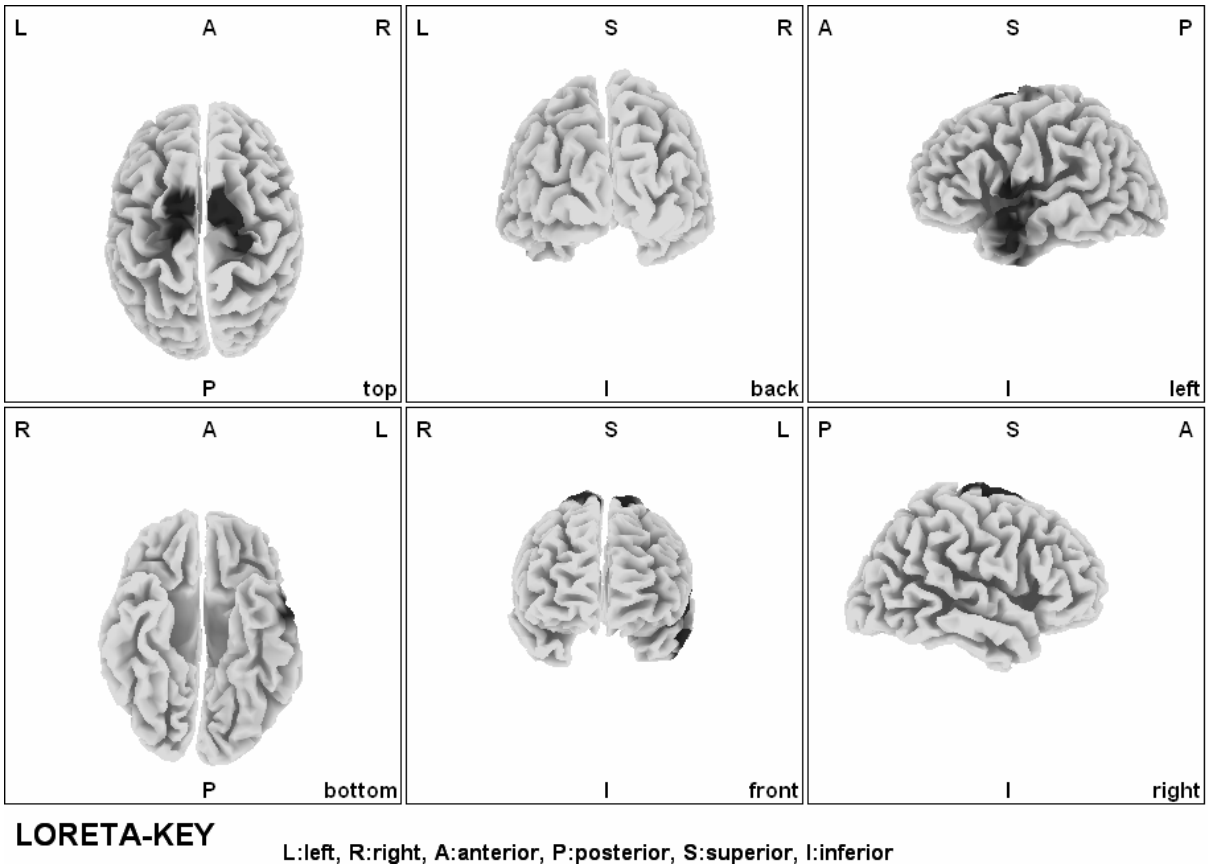

Figure 11.17: LORETA functional images of regional electric activity differences for the comparison "DOWN minus CONTROL" in children. Depicted in black color is the increased Theta power activity in the DOWN condition bilateral in the superior frontal gyrus and in the left temporal gyrus extending into the temporal pole. Note that increased Theta power in the superior frontal gyrus indicates decreased cortical activity in the DOWN condition; whereas increased Theta power in the temporal lobe indicates increased cortical activity in the DOWN condition (please see text and chapter 3.2.3.1 for an explanation). Results are displayed on the "fiducial cortical surface" (boundary midway through cortical thickness, Dickson et al., 2001). Cortex is shown in grey scale.

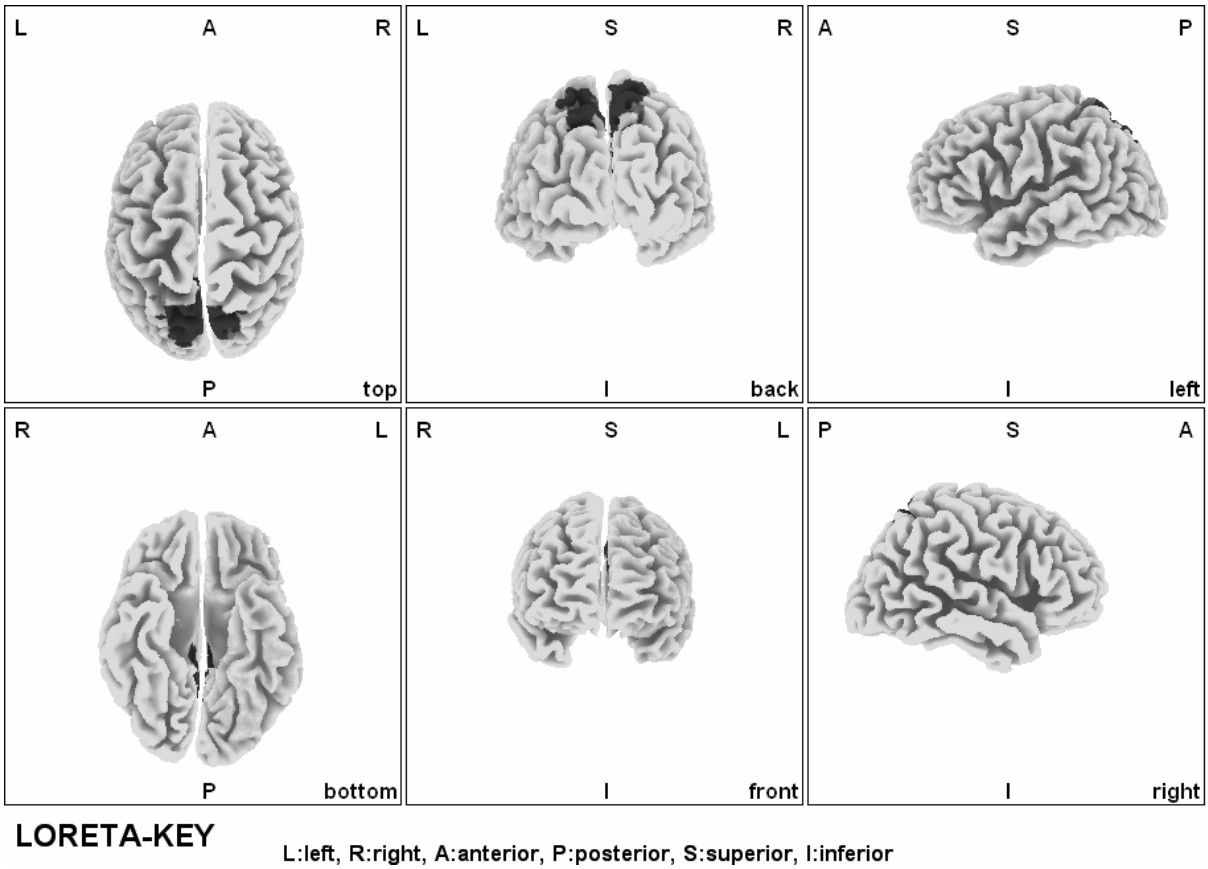

Figure 11.18: LORETA functional images of regional electric activity differences for the comparison "DOWN minus CONTROL" in adolescents. Depicted in black color is the increased Alpha power activity in the CONTROL condition bilateral in the parietal cortex (superior parietal gyrus, precuneus, posterior cingulate, cingulate gyrus), indicating increased brain activity in the DOWN condition in the parietal cortex (note that Alpha power is negatively correlated with activity). Results are displayed on the "fiducial cortical surface" (boundary midway through cortical thickness, Dickson et al., 2001). Cortex is shown in grey scale.

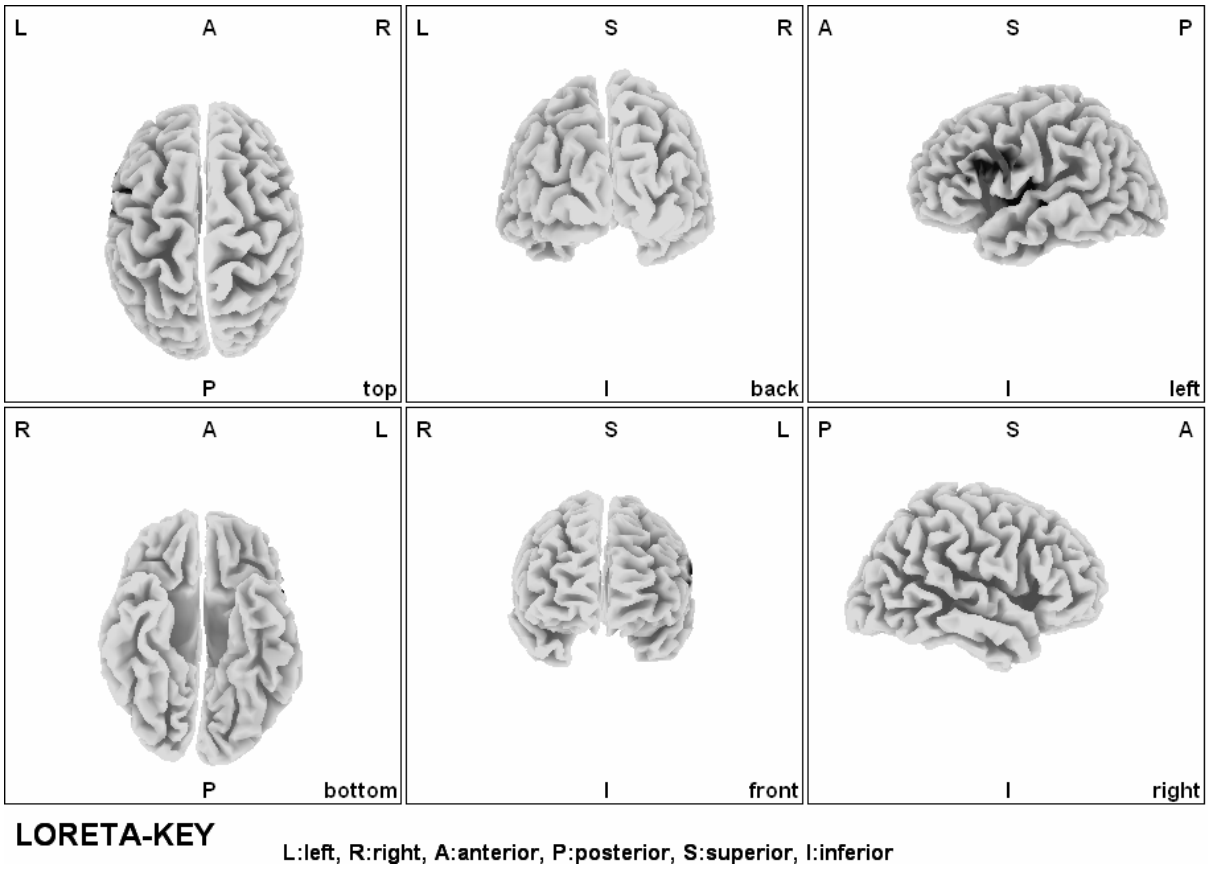

Figure 11.19: LORETA functional images of regional electric activity differences for the comparison "DOWN minus CONTROL" in adolescents. Depicted in black color is the increased Beta2 power activity in the DOWN condition in the left insula, the left inferior frontal gyrus and the left precentral gyrus, indicating increased brain activity in the DOWN condition in these brain areas (note that Beta2 power is positively correlated with activity). Results are displayed on the "fiducial cortical surface" (boundary midway through cortical thickness, Dickson et al., 2001). Cortex is shown in grey scale.

12 Curriculum vitae

Education:

1996-2002 University of Zurich, Faculty of Philosophy, Institute of Psychology, **Diploma in Psychology, Psychopathology and Neurophysiology (Master)**, Zurich, Switzerland

10/02-06/05 University of Zurich, Faculty of Philosophy, Institute of Psychology, Department of Neuropsychology, **Ph.D. in Neuroscience (summa cum laude)** Supervisor Prof. Dr. Lutz Jäncke, Zurich, Switzerland

Own publications:

Paper in peer reviewed journals:

Baumgartner, T., Esslen, M. & Jäncke, L. (in press). From emotion perception to emotion experience: Emotions evoked by pictures and classical music. *International Journal of Psychophysiology.*

Baumgartner, T., Valko, L., Esslen, M. & Jäncke, L. (in press). The neural correlate of Spatial Presence in an arousing and non-interactive virtual reality world – an EEG and Psychophysiology study. *CyberPsychology & Behavior.*

Baumgartner, T., Lutz, K., Schmidt, C. & Jäncke, L. (in press). The emotional power of music: How music enhances the feeling of affective pictures. *Cognitive Brain Research*.

Dey, M., Gschwend, B., **Baumgartner, T.**, Jäncke, P. & Jäncke L. (2006). Effekte von Musik auf das Fahrverhalten. *Zeitschrift für Verkehrssicherheit, 52,* 32-36.

Heinrichs, M., **Baumgartner, T.**, Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biol.Psychiatry, 54,* 1389-1398.

Book chapters:

Baumgartner, T., Esslen, M. & Jäncke, L. (2004). From emotion perception to emotion experience: Emotions evoked by pictures and classical music. *Extended abstract for the Annual Meeting Press Book of the Society for Neuroscience.*

Heinrichs, M., **Baumgartner, T.**, Kirschbaum, C., Ehlert, U. & Hellhammer, D. H. (2002).

Neurobiologie und Psychosomatik: Mechanismen von Stressprotektion beim Menschen. In D. Mattke, G. Hertel, S. Büsing & K. Schreiber-Willnow (Hrsg.), *Störungsspezifische Konzepte und Behandlung in der Psychosomatik* (S. 328-336). Frankfurt: VAS.

Talks at conventions

Baumgartner, T., Heinrichs, M., Kirschbaum, C., Ehlert, U. & Hellhammer, D. H. (2001). Soziale Unterstützung und Stress: Welches sind die protektiven Mechanismen aus psychoendokrinologischer Perspektive? 8. Kongress der Deutschen Gesellschaft für Verhaltensmedizin und Verhaltensmodifikation (DGVM), Kiel.

Poster presentations

Baumgartner, T., Lutz, K., Schmid, C. & Jäncke, L. (2005). The emotional power of music: How music enhances the feeling of affective pictures. ZNZ-Symposium 2005, Centre for Neuroscience Zurich, Zurich.

Baumgartner, T., Esslen, M. & Jäncke, L. (2004). From emotion perception to emotion experience: Emotions evoked by affective pictures and classical music. Congress of the Society for Neuroscience, San Diego (USA), October 2004.

Baumgartner, T., Heinrichs, M., Ehlert, U., Kirschbaum, C. & Hellhammer, D. H. (2000). Effects of oxytocin and social support on psychoendocrine stress responsiveness in healthy men. ZNZ-Symposium 2000, Centre for Neuroscience Zurich, Zurich.

Teaching experience at the University of Zurich

Methodenpropädeutikum der Neuropsychologie SS 2003
Methodenpropädeutikum der Neuropsychologie SS 2004
Affektive Neurowissenschaften SS 2004
Affektive Neurowissenschaften WS 2004
Affektive Neurowissenschaften SS2005
Affektive Neurowissenschaften WS 2005
Blockkurs neuropsychologische Methoden WS 2004